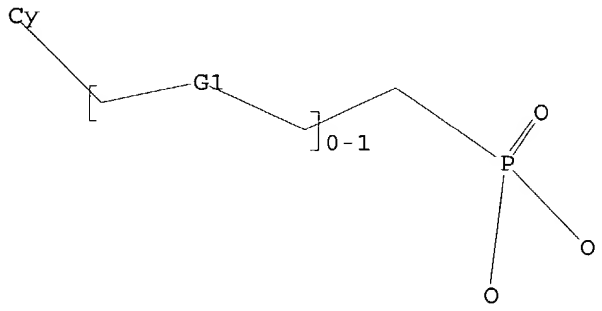
L1 STRUCTURE UPLOADED

=> d
L1 HAS NO ANSWERS
L1 STR



G1 O,S,N

Structure attributes must be viewed using STN Express query preparation.

=> s l1
SAMPLE SEARCH INITIATED 14:52:10 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 7923 TO ITERATE

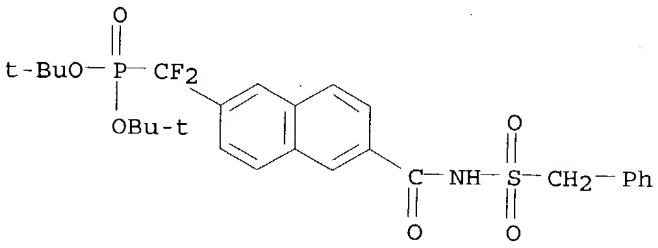
12.6% PROCESSED 1000 ITERATIONS 50 ANSWERS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 153126 TO 163794
PROJECTED ANSWERS: 29152 TO 33914

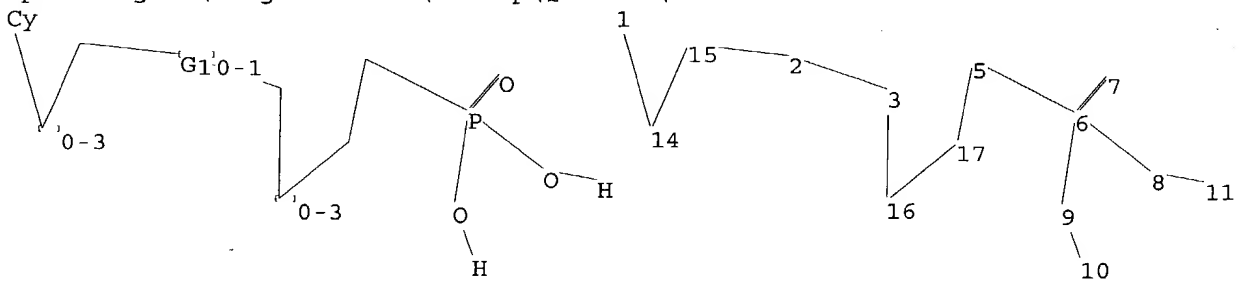
L2 50 SEA SSS SAM L1

=> d scan

L2 50 ANSWERS REGISTRY COPYRIGHT 2004 ACS on STN
IN Phosphonic acid, [difluoro[6-[[[(phenylmethyl)sulfonyl]amino]carbonyl]-2-naphthalenyl]methyl]-, bis(1,1-dimethylethyl) ester (9CI)
MF C27 H32 F2 N O6 P S



=>
Uploading C:\Program Files\Stnexp\Queries\09406269.str



chain nodes :
1 2 3 5 6 7 8 9 10 11 14 15 16 17
chain bonds :
1-14 2-3 2-15 3-16 5-6 5-17 6-7 6-8 6-9 8-11 9-10 14-15 16-17
exact/norm bonds :
1-14 2-3 2-15
exact bonds :
3-16 5-6 5-17 8-11 9-10 14-15 16-17
normalized bonds :
6-7 6-8 6-9

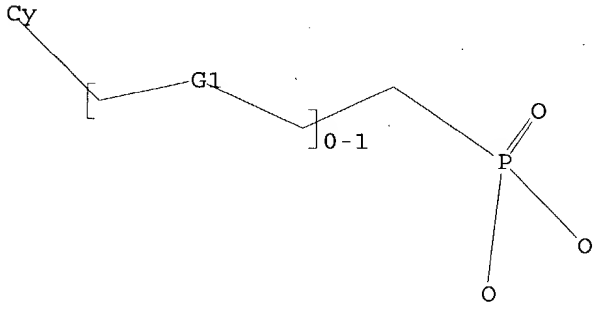
G1:O,S,N

Match level :
1:Atom 2:CLASS 3:CLASS 5:CLASS 6:CLASS 7:CLASS 8:CLASS 9:CLASS 10:CLASS
11:CLASS 14:CLASS 15:CLASS 16:CLASS 17:CLASS

L3 STRUCTURE UPLOADED

=> sd
SD IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).

=> d
L3 HAS NO ANSWERS
L3 STR



G1 O,S,N

Structure attributes must be viewed using STN Express query preparation.

=>

=> s l3
SAMPLE SEARCH INITIATED 14:55:28 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 7923 TO ITERATE

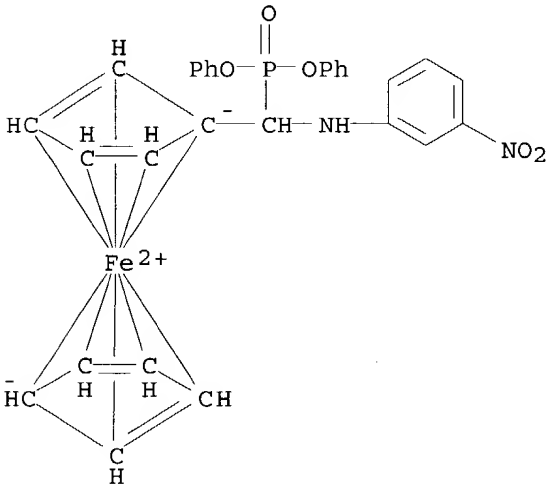
12.6% PROCESSED 1000 ITERATIONS 50 ANSWERS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 153126 TO 163794
PROJECTED ANSWERS: 29152 TO 33914

L4 50 SEA SSS SAM L3

=> d scan

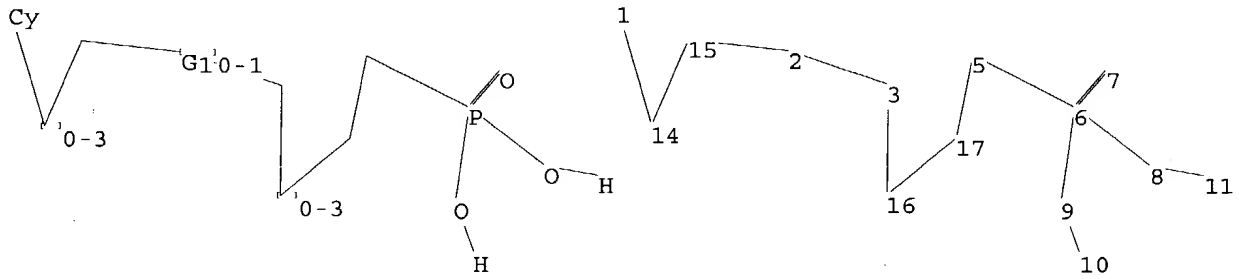
L4 50 ANSWERS REGISTRY COPYRIGHT 2004 ACS on STN
IN Ferrocene, [(diphenoxyphosphinyl)[(3-nitrophenyl)amino]methyl]- (9CI)
MF C29 H25 Fe N2 O5 P
CI CCS



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):0

=>
Uploading C:\Program Files\Stnexp\Queries\09406269.str



chain nodes :
1 2 3 5 6 7 8 9 10 11 14 15 16 17
chain bonds :
1-14 2-3 2-15 3-16 5-6 5-17 6-7 6-8 6-9 8-11 9-10 14-15 16-17
exact/norm bonds :
1-14 2-3 2-15
exact bonds :
3-16 5-6 5-17 8-11 9-10 14-15 16-17
normalized bonds :
6-7 6-8 6-9

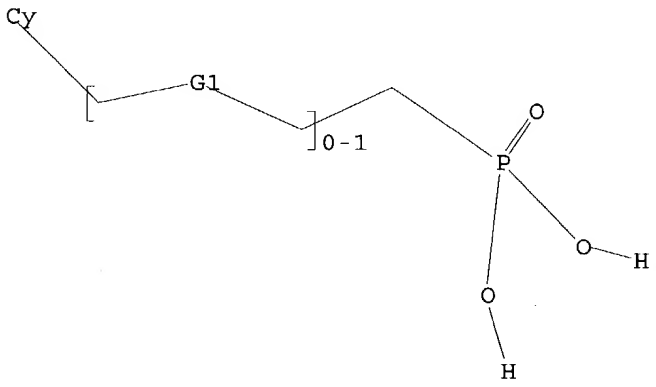
G1:O,S,N

Match level :
1:Atom 2:CLASS 3:CLASS 5:CLASS 6:CLASS 7:CLASS 8:CLASS 9:CLASS 10:CLASS
11:CLASS 14:CLASS 15:CLASS 16:CLASS 17:CLASS

L5 STRUCTURE UPLOADED

=>

=> d
L5 HAS NO ANSWERS
L5 STR



G1 O,S,N

Structure attributes must be viewed using STN Express query preparation.

=> s l5
SAMPLE SEARCH INITIATED 14:56:58 FILE 'REGISTRY'

SAMPLE SCREEN SEARCH COMPLETED - 2076 TO ITERATE

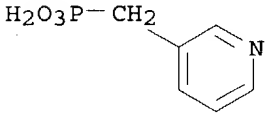
48.2% PROCESSED 1000 ITERATIONS 50 ANSWERS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 38788 TO 44252
PROJECTED ANSWERS: 6084 TO 8364

L6 50 SEA SSS SAM L5

=> d scan

L6 50 ANSWERS REGISTRY COPYRIGHT 2004 ACS on STN
IN Phosphonic acid, (3-pyridinylmethyl)-, monohydrate (9CI)
MF C6 H8 N O3 P . H2 O



● H_2O

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):0

=> s l5 full
FULL SEARCH INITIATED 14:57:32 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 41678 TO ITERATE

100.0% PROCESSED 41678 ITERATIONS 6573 ANSWERS
SEARCH TIME: 00.00.01

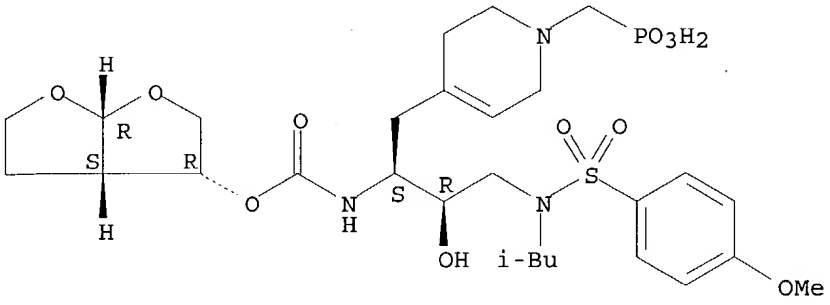
L7 6573 SEA SSS FUL L5

=> s l7 not m/els
3578042 M/ELS
L8 5741 L7 NOT M/ELS

=> d scan

L8 5741 ANSWERS REGISTRY COPYRIGHT 2004 ACS on STN
IN Carbamic acid, [(1S,2R)-2-hydroxy-3-[[(4-methoxyphenyl)sulfonyl](2-methylpropyl)amino]-1-[[1,2,3,6-tetrahydro-1-(phosphonomethyl)-4-pyridinyl]methyl]propyl]-, C-[(3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl] ester (9CI)
MF C28 H44 N3 O11 P S

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):0

=> file caplus

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	163.63	164.68

FILE 'CAPLUS' ENTERED AT 14:58:13 ON 03 MAY 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907 - 3 May 2004 VOL 140 ISS 19
FILE LAST UPDATED: 2 May 2004 (20040502/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

```
=> s l8 and pharmaceut?
          2956 L8
        246787 PHARMACEUT?
L9         172 L8 AND PHARMACEUT?

=> s l9 and (blood or thrombo?)
       1131789 BLOOD
          1163 BLOODS
       1131904 BLOOD
                  (BLOOD OR BLOODS)
         66936 THROMBO?
L10         18 L9 AND (BLOOD OR THROMBO?)

=> s l10 and coagul?
        129369 COAGUL?
L11          0 L10 AND COAGUL?
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```
=> d ti 1-18
L11 HAS NO ANSWERS
'TI ' IS NOT A VALID STRUCTURE FORMAT KEYWORD
Structure Formats
SIA ----- Structure Image, Attributes, and map table if it contains
          data.  (Default)
SIM ----- Structure IMage.
SAT ----- Structure ATtributes and map table if it contains data.
SCT ----- Structure Connection Table and map table if it contains
          data.
SDA ----- All Structure DAta (image, attributes, connection table and
          map table if it contains data).
NOS ----- NO Structure data.
ENTER STRUCTURE FORMAT (SIA), SCT, SDA, SIM, SAT, NOS:end

=> d ti 1-18 l10

L10  ANSWER 1 OF 18  CAPLUS  COPYRIGHT 2004 ACS on STN
TI   Preparation of N-phenyl or N-heterocyclyldibenzylamine compounds as
     inhibitors of cholesteryl ester transfer protein (CETP) and medicinal use
     thereof

L10  ANSWER 2 OF 18  CAPLUS  COPYRIGHT 2004 ACS on STN
TI   Preparation of quinoline derivatives as TGFβ inhibitors

L10  ANSWER 3 OF 18  CAPLUS  COPYRIGHT 2004 ACS on STN
TI   Phosphonate-substituted non-nucleoside reverse transcriptase inhibitors
     (NNRTIs)

L10  ANSWER 4 OF 18  CAPLUS  COPYRIGHT 2004 ACS on STN
TI   Preparation and compositions of nitrosothio (hetero)cyclic nitric oxide
     donors

L10  ANSWER 5 OF 18  CAPLUS  COPYRIGHT 2004 ACS on STN
TI   Substituted piperazine antithrombotic PAI-1 (plasminogen activator
     inhibitor-1) inhibitors, and their preparation, pharmaceutical
     compositions, and use in the treatment of thrombotic diseases.

L10  ANSWER 6 OF 18  CAPLUS  COPYRIGHT 2004 ACS on STN
TI   Preparation of 1-phenyl-2,5-imidazolidinediones and analogs for treatment
     of inflammatory and immune cell-mediated diseases

L10  ANSWER 7 OF 18  CAPLUS  COPYRIGHT 2004 ACS on STN
TI   Compounds and methods for modulating cerebral amyloid angiopathy using
     inhibitors of an amyloid β peptide

L10  ANSWER 8 OF 18  CAPLUS  COPYRIGHT 2004 ACS on STN
TI   Preparation of substituted guanidine derivatives as inhibitors of
     sodium/proton exchange transport system

L10  ANSWER 9 OF 18  CAPLUS  COPYRIGHT 2004 ACS on STN
TI   Phosphonated agents and their antiangiogenic and antitumorigenic use

L10  ANSWER 10 OF 18  CAPLUS  COPYRIGHT 2004 ACS on STN
TI   CMP derivative sialyltransferase inhibitors, preparation,
     pharmaceutical compositions, and therapeutic use

L10  ANSWER 11 OF 18  CAPLUS  COPYRIGHT 2004 ACS on STN
TI   Inhibitors of the interaction of glutamate with the AMPA and/or kainate
     receptor complex for treatment of demyelinating disorders

L10  ANSWER 12 OF 18  CAPLUS  COPYRIGHT 2004 ACS on STN
TI   Phosphonated agents and their antiangiogenic and antitumorigenic use
```

L10 ANSWER 13 OF 18 CAPLUS COPYRIGHT 2004 ACS on STN
TI Preparation of mixed benzene boron and phosphorus acid derivatives and **pharmaceutical** compositions useful as angiogenesis inhibitors

L10 ANSWER 14 OF 18 CAPLUS COPYRIGHT 2004 ACS on STN
TI IRC011, a new synthetic chelator with selective interaction with catabolic red **blood** cell iron: evaluation in hypertransfused rats with hepatocellular and reticuloendothelial radioiron probes and in iron-loaded rat heart cells in culture

L10 ANSWER 15 OF 18 CAPLUS COPYRIGHT 2004 ACS on STN
TI Radiopharmaceutical formulations, their method of administration and process of preparation

L10 ANSWER 16 OF 18 CAPLUS COPYRIGHT 2004 ACS on STN
TI Method of treating cerebral ischemia using 4-(phosphonoalkyl- or -alkenyl)piperazine-2-carboxylic acids and their salts, esters and amides

L10 ANSWER 17 OF 18 CAPLUS COPYRIGHT 2004 ACS on STN
TI Novel bisphosphonic acid derivatives, a method for their production and **pharmaceutical** compositions containing them

L10 ANSWER 18 OF 18 CAPLUS COPYRIGHT 2004 ACS on STN
TI Diphosphonate derivatives and **pharmaceutical** compositions containing them

=> d ibib abs hitstr 5
L11 HAS NO ANSWERS
'IBIB ABS HITSTR ' IS NOT A VALID STRUCTURE FORMAT KEYWORD
Structure Formats
SIA ----- Structure Image, Attributes, and map table if it contains data. (Default)
SIM ----- Structure IMage.
SAT ----- Structure ATtributes and map table if it contains data.
SCT ----- Structure Connection Table and map table if it contains data.
SDA ----- All Structure DAta (image, attributes, connection table and map table if it contains data).
NOS ----- NO Structure data.
ENTER STRUCTURE FORMAT (SIA), SCT, SDA, SIM, SAT, NOS:end

=> d ibib abs hitstr 5 l10

L10 ANSWER 5 OF 18 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:777592 CAPLUS
DOCUMENT NUMBER: 139:292270
TITLE: Substituted piperazine antithrombotic PAI-1 (plasminogen activator inhibitor-1) inhibitors, and their preparation, **pharmaceutical** compositions, and use in the treatment of **thrombotic** diseases.
INVENTOR(S): Chou, Yuo-Ling; Ghannam, Ameen; Kochanny, Monica J.; Lee, Wheeseong; Lu, Shou-Fu; Shaw, Kenneth J.; Ye, Bin; Zhao, Zuchun
PATENT ASSIGNEE(S): Schering Aktiengesellschaft, Germany
SOURCE: PCT Int. Appl., 61 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003080060	A1	20031002	WO 2003-US7508	20030313

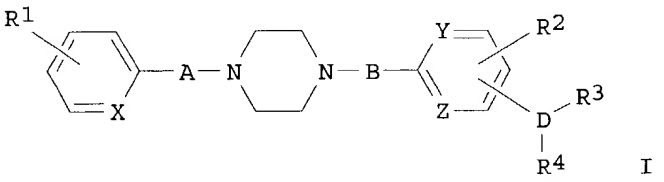
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

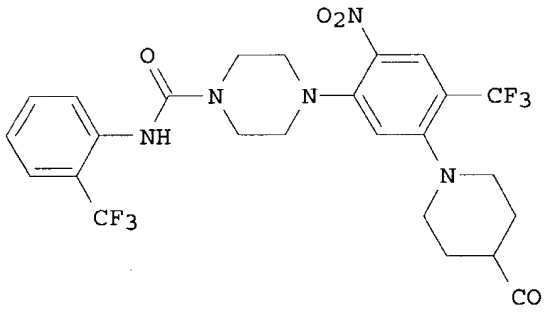
PRIORITY APPLN. INFO.: US 2002-365988P P 20020320

OTHER SOURCE(S): MARPAT 139:292270

GI



I



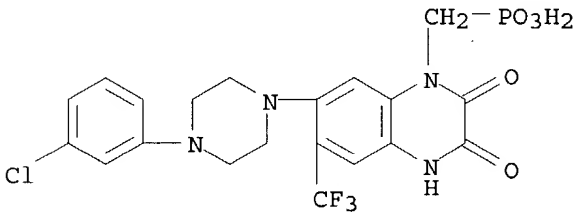
II

AB The invention is directed to substituted piperazine compds. I and their **pharmaceutically** acceptable salts, which are useful as antithrombotic agents by inhibiting plasminogen activator inhibitor-1 (PAI-1) [wherein: R1 = (one or more) H, haloalkyl, halo, or NO2; X, Y, Z = (independently) C or N; A = bond, CH2, CO, or alkylaminocarbonyl; B = bond, alkylaminocarbonyl, CH2, or carbonylalkylester (sic); R2 = halo, NO2, CO2H or alkyl ester, haloalkyl, dialkylamide, carboxamide, alkoxyaminocarbonyl, substituted aralkylamino, aryloxy, piperazinyl, imidazolyl, or pyridinyloxy, etc.; D = N or O; R3 = (un)substituted aryl, aralkyl, carboxycyclohexyl, carboxyalkyl, piperazinyl, alkoxy, aralkoxy, carboxypyrrolidinyl, carboxypiperidinyl, carboxypyridinyloxy, carboxypyridinyl; R4 = halo, NO2, CO2H, alkyl, alkyl ester, haloalkyl, menthyloxyalkylcarbonylamino, aralkylamino, etc.; or DR3R4 = atoms to form (un)substituted piperidine or pyrrolidine ring; or R2R3 = atoms to form dioxo-substituted heterocyclic group substituted by methylphosphonic acid (when Y = Z = C); including stereoisomers and/or **pharmaceutically** acceptable salts]. In addition, the invention relates to **pharmaceutical** compns., and methods of using the compds. to treat disease-states characterized by **thrombotic** activity. Over 100 compds. are listed, all of which inhibited human PAI-1 either in vitro

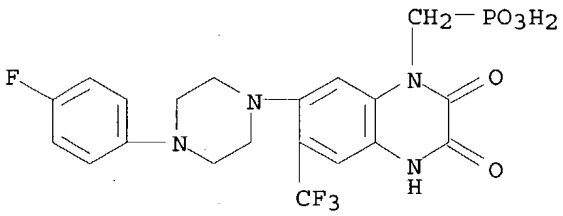
(recombinant PAI-1 chromogenic hydrolysis assay), ex vivo (human plasma fibrin clot lysis assay), or both, with IC50 values of less than about 15 μM. Ten formulations of invention compound II are listed. Seven synthetic prepns. are described. For instance, 2,4-dichloro-5-nitrobenzotrifluoride was doubly aminated, first with N-BOC-piperazine in the 4-position, then with Et isonipecotate in the 2-position, followed by deprotection of the BOC-protected amine, carbamoylation of the amine with 2-(trifluoromethyl)phenyl isocyanate, and saponification of the ester with LiOH in aqueous THF, to give compound II.

IT **608530-74-1P**, [[7-[4-(3-Chlorophenyl)piperazin-1-yl]-2,3-dioxo-6-trifluoromethyl-3,4-dihydro-2H-quinoxalin-1-yl]methyl]phosphonic acid
608530-75-2P, [[7-[4-(4-Fluorophenyl)piperazin-1-yl]-2,3-dioxo-6-trifluoromethyl-3,4-dihydro-2H-quinoxalin-1-yl]methyl]phosphonic acid
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of [(triphenylmethyl)phenyl]piperazines as antithrombotic PAI-1 inhibitors)

RN 608530-74-1 CAPLUS
CN Phosphonic acid, [[7-[4-(3-chlorophenyl)-1-piperazinyl]-3,4-dihydro-2,3-dioxo-6-(trifluoromethyl)-1(2H)-quinoxalinyl]methyl]- (9CI) (CA INDEX NAME)



RN 608530-75-2 CAPLUS
CN Phosphonic acid, [[7-[4-(4-fluorophenyl)-1-piperazinyl]-3,4-dihydro-2,3-dioxo-6-(trifluoromethyl)-1(2H)-quinoxalinyl]methyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d ibib abs hitstr 10-18 l10

L10 ANSWER 10 OF 18 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:117065 CAPLUS
DOCUMENT NUMBER: 132:161274
TITLE: CMP derivative sialyltransferase inhibitors, preparation, **pharmaceutical** compositions, and therapeutic use
INVENTOR(S): Schmidt, Richard R.; Schaub, Christoph; Muller, Bernd; Amann, Franz
PATENT ASSIGNEE(S): Germany
SOURCE: PCT Int. Appl., 63 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000008040	A1	20000217	WO 1999-EP5697	19990806
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9960791	A1	20000228	AU 1999-60791	19990806

PRIORITY APPLN. INFO.: US 1998-95700P P 19980807
WO 1999-EP5697 W 19990806

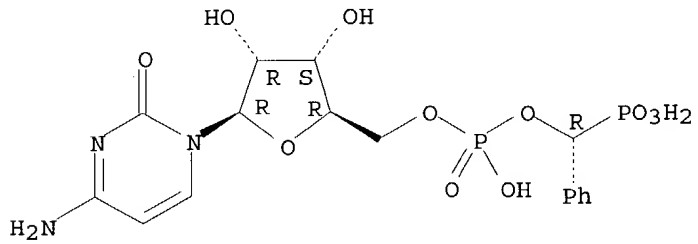
OTHER SOURCE(S): MARPAT 132:161274

AB The invention provides potent inhibitors of sialyltransferases. The sialyltransferase inhibitors are useful for inhibiting the synthesis of sialylated glycosides. The sialyltransferase inhibitors find use in the modulation of biol. processes that involve sialyl glycoside-mediated cell adhesion. The compds. of the invention may be used e.g. to treat inflammation.

IT **258857-06-6P 258857-07-7P 258857-08-8P**
258857-09-9P 258857-13-5P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(CMP derivative sialyltransferase inhibitors, preparation, **pharmaceutical** compns., and therapeutic use)

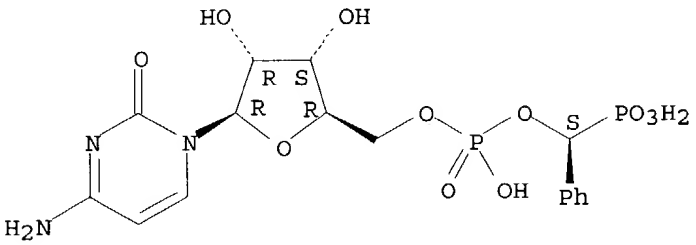
RN 258857-06-6 CAPLUS
CN 5'-Cytidylic acid, mono[(R)-phenylphosphonomethyl] ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



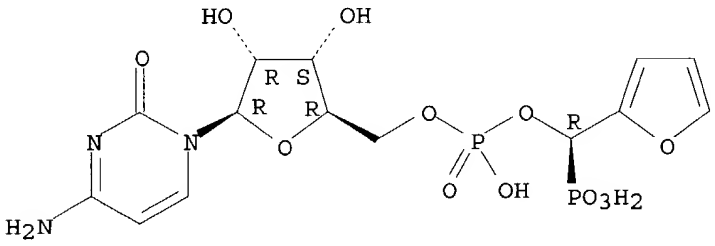
RN 258857-07-7 CAPLUS
CN 5'-Cytidylic acid, mono[(S)-phenylphosphonomethyl] ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



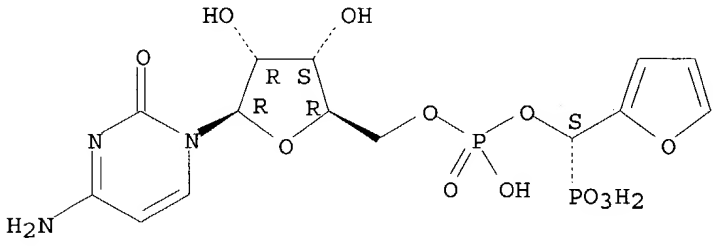
RN 258857-08-8 CAPLUS
CN 5'-Cytidylic acid, mono[(R)-2-furanylphosphonomethyl] ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



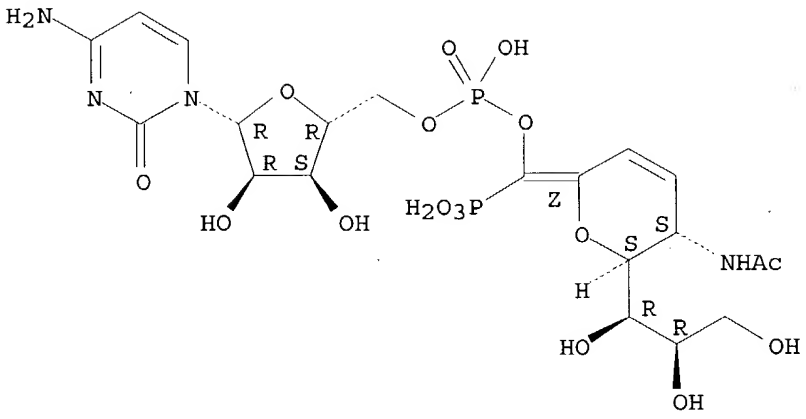
RN 258857-09-9 CAPLUS
CN 5'-Cytidylic acid, mono[(S)-2-furanylphosphonomethyl] ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



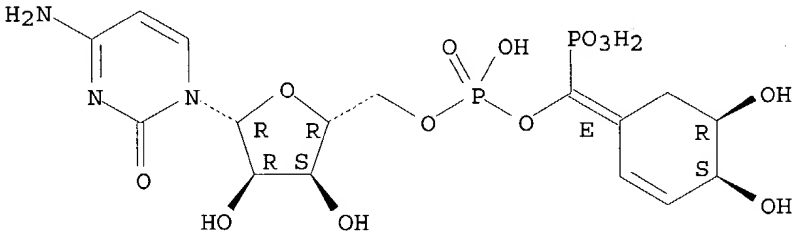
RN 258857-13-5 CAPLUS
CN 5'-Cytidylic acid, 1-ester with (1Z)-5-(acetylamino)-2,6-anhydro-3,4,5-trideoxy-1-C-phosphono-D-manno-non-1,3-dienitol (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



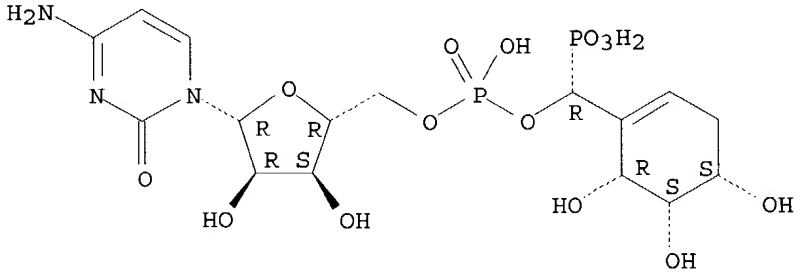
IT **258857-14-6 258860-27-4 258860-28-5**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(CMP derivative sialyltransferase inhibitors, preparation, **pharmaceutical** compns., and therapeutic use)
RN 258857-14-6 CAPLUS
CN 5'-Cytidylic acid, mono[(E)-[(4S,5R)-4,5-dihydroxy-2-cyclohexen-1-ylidene]phosphonomethyl] ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 258860-27-4 CAPLUS
CN 5'-Cytidylic acid, mono[(R)-phosphono[(4S,5S,6R)-4,5,6-trihydroxy-1-cyclohexen-1-yl]methyl] ester (9CI) (CA INDEX NAME)

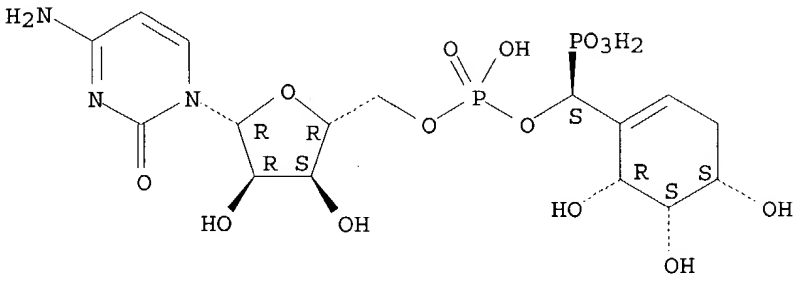
Absolute stereochemistry.



RN 258860-28-5 CAPLUS
CN 5'-Cytidylic acid, mono[(S)-phosphono[(4S,5S,6R)-4,5,6-trihydroxy-1-

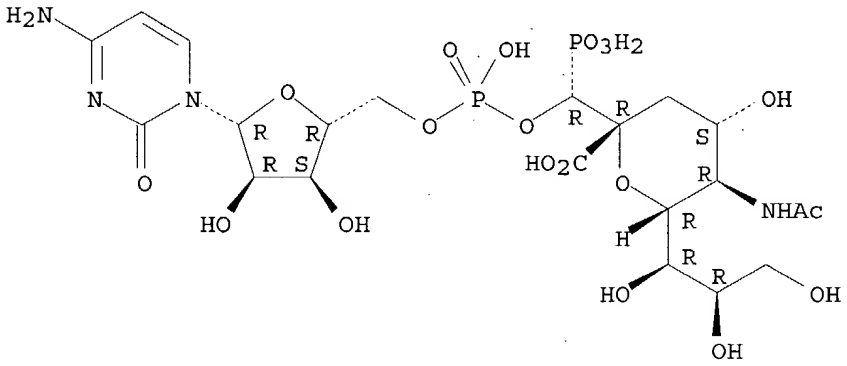
cyclohexen-1-yl]methyl] ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **258857-05-5**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(CMP derivative sialyltransferase inhibitors, preparation, **pharmaceutical** compns., and therapeutic use)
RN 258857-05-5 CAPLUS
CN D-erythro-L-manno-Nononic acid, 5-(acetylamino)-2,6-anhydro-2-C-[(R)-(5'-cytidylyloxy)phosphonomethyl]-3,5-dideoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 11 OF 18 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:34733 CAPLUS
DOCUMENT NUMBER: 132:88184
TITLE: Inhibitors of the interaction of glutamate with the AMPA and/or kainate receptor complex for treatment of demyelinating disorders
INVENTOR(S): Turski, Lechoslaw; Smith, Terence
PATENT ASSIGNEE(S): Eisai Co., Ltd, Japan
SOURCE: PCT Int. Appl., 104 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

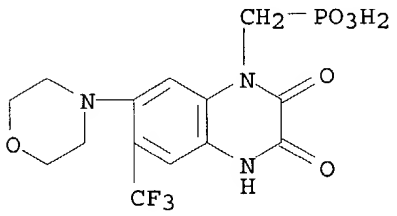
WO 2000001376	A2	20000113	WO 1999-GB2112	19990702
WO 2000001376	A3	20010322		
W: JP, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 1100504	A2	20010523	EP 1999-929545	19990702
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2002519373	T2	20020702	JP 2000-557823	19990702

PRIORITY APPLN. INFO.: GB 1998-14380 A 19980702
GB 1998-24393 A 19981106
WO 1999-GB2112 W 19990702

AB New therapies can be devised based upon a demonstration of the role of glutamate in the pathogenesis of demyelinating disorders. Inhibitors of the interaction of glutamate with the AMPA and/or kainate receptor complex are likely to be useful in treating demyelinating disorders and can be formulated as **pharmaceutical** compns.

IT **161605-73-8**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhibitors of interaction of glutamate with AMPA and/or kainate receptor complex for treatment of demyelinating disorders)

RN 161605-73-8 CAPLUS
CN Phosphonic acid, [[3,4-dihydro-7-(4-morpholinyl)-2,3-dioxo-6-(trifluoromethyl)-1(2H)-quinoxalinyl]methyl]- (9CI) (CA INDEX NAME)



L10 ANSWER 12 OF 18 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:96248 CAPLUS
DOCUMENT NUMBER: 130:148689
TITLE: Phosphonated agents and their antiangiogenic and antitumorigenic use
INVENTOR(S): Collins, Delwood C.; Gagliardi, Antonio R.; Nickel, Peter
PATENT ASSIGNEE(S): University of Kentucky Research Foundation, USA
SOURCE: PCT Int. Appl., 74 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9905148	A1	19990204	WO 1998-US15470	19980724
W: AU, CA, JP, MX				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9885915	A1	19990216	AU 1998-85915	19980724
AU 739637	B2	20011018		

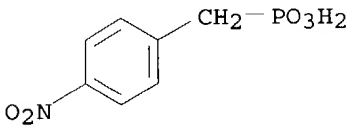
EP 1019419 A1 20000719 EP 1998-937133 19980724
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI
PRIORITY APPLN. INFO.: US 1997-899996 A 19970724
WO 1998-US15470 W 19980724

OTHER SOURCE(S): MARPAT 130:148689

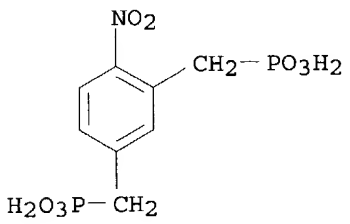
AB The present invention relates to novel phosphonic acid substituted agents and their **pharmaceutical** compns. Phosphonic acid substituted agents that are potent inhibitors of angiogenesis or tumorigenesis is defined by the following formula: (P-Yn1)m1-Q1-K-(Q2-(Yn2-P)m2)j (P = phosphonic group, phosphonic salt; Y = OCO, NR1CO, CON(R1)R2; Q1, Q2 = aryl; K = H, NHCONH, NHCSNH, NHCOR3, NHCSR3CSNH; j, n1, n2 = 0-2; m1, m2 = 1-4; R1 = H, CH2CO2H, alkyl; R2 = alkyl, aryl, alkaryl; R3 = aryl). A **pharmaceutical** composition for the treatment of angiogenesis-dependent conditions or tumors comprises an effective amount of a phosphonic acid agent and a **pharmaceutically** acceptable carrier. Some of the phosphonic acid agents were more potent inhibitors of angiogenesis in the chick chorioallantoic membrane (CAM) assay and to human microvascular endothelial cell growth than suramin.

IT **1205-62-5P 220240-22-2P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(phosphonic acid agents and their antiangiogenic and antitumorigenic use)

RN 1205-62-5 CAPLUS
CN Phosphonic acid, [(4-nitrophenyl)methyl]- (9CI) (CA INDEX NAME)



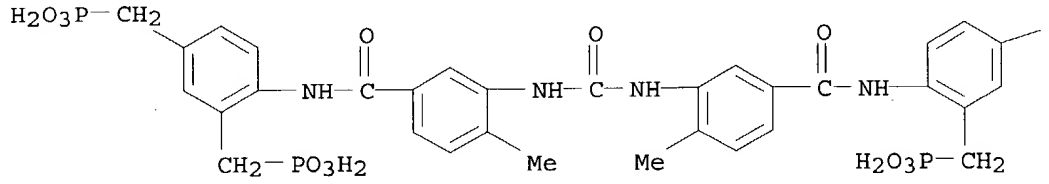
RN 220240-22-2 CAPLUS
CN Phosphonic acid, [(4-nitro-1,3-phenylene)bis(methylene)]bis- (9CI) (CA INDEX NAME)



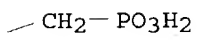
IT **220239-98-5**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(phosphonic acid agents and their antiangiogenic and antitumorigenic use)

RN 220239-98-5 CAPLUS
CN Phosphonic acid, [carbonylbis[imino(4-methyl-3,1-phenylene)carbonylimino-1,2,4-benzenetriylbis(methylene)]]tetrakis- (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 1-B



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 13 OF 18 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:509201 CAPLUS
DOCUMENT NUMBER: 129:149098
TITLE: Preparation of mixed benzene boron and phosphorus acid derivatives and **pharmaceutical** compositions useful as angiogenesis inhibitors
INVENTOR(S): Cordi, Alex; Desos, Patrice; Morris, Angela D.; Atassi, Ghanem; Pierre, Alain
PATENT ASSIGNEE(S): Adir et Cie., Fr.
SOURCE: PCT Int. Appl., 79 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9831689	A1	19980723	WO 1998-FR90	19980119
W: AU, BR, CA, CN, HU, JP, NO, NZ, PL, US				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
FR 2758562	A1	19980724	FR 1997-526	19970120
FR 2758562	B1	19990219		
AU 9859931	A1	19980807	AU 1998-59931	19980119
ZA 9800441	A	19980729	ZA 1998-441	19980120
PRIORITY APPLN. INFO.:			FR 1997-526	19970120
			WO 1998-FR90	19980119

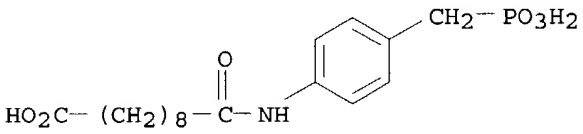
OTHER SOURCE(S): CASREACT 129:149098; MARPAT 129:149098

AB The invention concerns the preparation and pharmacol. usefulness of R1R2R3C6H2A2NRaXA1XNRbA3C6H2R'1R'2R4 (R1, R2, R'1, R'2 = H, halogen, C1-6 alkyl, C1-6 alkoxy, hydroxy, nitro, trihalomethyl; or R1 and R2 (or R'1 and R'2) form together with the benzene nucleus which bears them a naphthyl or anthracenyl group; X = C:T, SO2, CH2, or X-A1-X = C(T)NHA1NHC(T) (T = O, S); A1 = C1-20 linear or branched alkylene chain with 0-6 double bonds in which ≥1 CH2 groups are replaced by O, S, CF2, phenylene, naphthylene, anthracenylene, cycloalkylene, 1,4-piperazinediyl, etc.; A2, A3 = alkylene group or single bond; R3 = H, halogen, NO2, CN, trihalomethyl, C1-6 alkyl, aryl, acyl, A4P(O)(OR6)(OR7) (A4 = single bond, alkylene), A4B(YR8)2 (Y = O, NR9; R9 = H, C1-6 alkyl); R4 = A4P(O)(OR6)(OR7), A4B(YR8)2 but R3 and R4 not both A4B(YR8)2; Ra, Rb = H, C1-6 alkyl). The invention also concerns isomers as well as additive salts to a **pharmaceutically** acceptable base. In an example

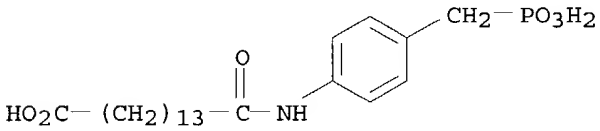
preparation, 4-(3-MeO2CC6H4NHC(O)(CH2)8C(O)NH)C6H4P(O)(OH)2 was obtained in 4 steps: 17.4 mmol of 4-H2NC6H4P(O)(OEt)2 were reacted with 17.4 mmol monomethyl sebacate, 17.4 mmol HATU and 43.5 mmol iPr2NEt in 150 mL CH2Cl2 to give MeO2C(CH2)8C(O)NH(C6H4P(O)(OEt)2-4) on workup; this intermediate was converted using KOH/H2O/MeOH to HO2C(CH2)8C(O)NH(C6H4P(O)(OEt)2-4), which was reacted with 3-H2NC6H4CO2Me in the presence of HATU and iPr2NEt in CH2Cl2 to give 4-(3-MeO2CC6H4NHC(O)(CH2)8C(O)NH)C6H4P(O)(OEt)2; finally the diester was converted to the acid using BrSiMe3 in MeCN. The above compds. are useful as angiogenesis inhibitors. Expts. are reported indicating that the compds. are powerful inhibitors of proliferation of endothelial cells and that they inhibit growth of M 5076 sarcoma in mice.

IT **210776-14-0P**, 9-((4-Phosphonomethylphenyl)carbamoyl)nonanoic acid **210776-16-2P**, 14-((4-(Phosphonomethyl)phenyl)carbamoyl)tetradecanoic acid **210776-25-3P**, Ethyl 9-((4-(ethoxy(phosphono)methyl)phenyl)carbamoyl)nonanoate **210776-27-5P**, 9-((4-(Ethoxy(phosphono)methyl)phenyl)carbamoyl)nonanoic acid
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate for preparation of mixed benzene boron and phosphorus acid derivs. as angiogenesis inhibitors)

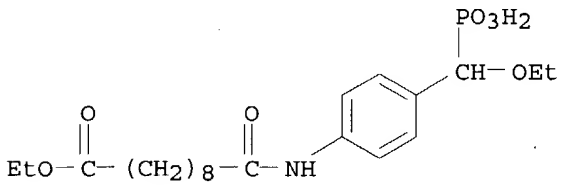
RN 210776-14-0 CAPLUS
CN Decanoic acid, 10-oxo-10-[[4-(phosphonomethyl)phenyl]amino]- (9CI) (CA INDEX NAME)



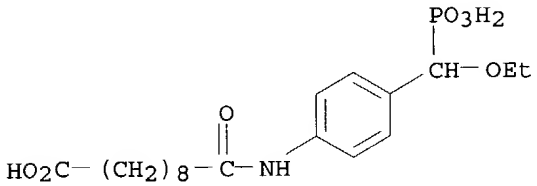
RN 210776-16-2 CAPLUS
CN Pentadecanoic acid, 15-oxo-15-[[4-(phosphonomethyl)phenyl]amino]- (9CI) (CA INDEX NAME)



RN 210776-25-3 CAPLUS
CN Decanoic acid, 10-[[4-(ethoxyphosphonomethyl)phenyl]amino]-10-oxo-, 1-ethyl ester (9CI) (CA INDEX NAME)



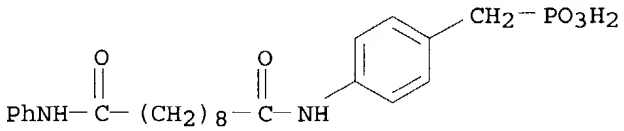
RN 210776-27-5 CAPLUS
CN Decanoic acid, 10-[[4-(ethoxyphosphonomethyl)phenyl]amino]-10-oxo- (9CI) (CA INDEX NAME)



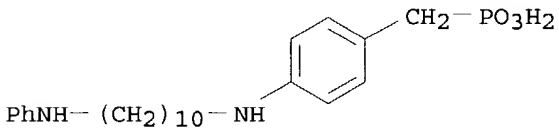
IT **210775-03-4P**, ((4-((9-(Phenylcarbamoyl)nonanoyl)amino)phenyl)methyl)phosphonic acid **210775-04-5P**, ((4-((10-(Phenylamino)decyl)amino)phenyl)methyl)phosphonic acid **210775-11-4P**, ((4-((13-(Phenylcarbamoyl)tridecanoyl)amino)phenyl)methyl)phosphonic acid **210775-13-6P**, ((4-((9-((2-Naphthyl)carbamoyl)nonanoyl)amino)phenyl)methyl)phosphonic acid **210775-19-2P**, ((4-(9-((4-Tolyl)carbamoyl)nonanoylamino)phenyl)methyl)phosphonic acid **210775-20-5P**, ((4-((9-((1-Naphthyl)carbamoyl)nonanoyl)amino)phenyl)methyl)phosphonic acid **210775-21-6P**, ((4-((9-((3-Biphenylyl)carbamoyl)nonanoyl)amino)phenyl)methyl)phosphonic acid **210775-22-7P**, ((4-((9-((4-Biphenylyl)carbamoyl)nonanoyl)amino)phenyl)methyl)phosphonic acid **210775-24-9P**, ((4-(9-(Methyl(phenyl)carbamoyl)nonanoylamino)phenyl)methyl)phosphonic acid **210775-25-0P**, ((4-(9-((3-Nitrophenyl)carbamoyl)nonanoylamino)phenyl)methyl)phosphonic acid **210775-26-1P**, ((4-(9-((3-Tolyl)carbamoyl)nonanoylamino)phenyl)methyl)phosphonic acid **210775-27-2P**, ((4-(13-((3-Nitrophenyl)carbamoyl)tridecanoylamino)phenyl)methyl)phosphonic acid **210775-29-4P**, ((4-(9-((2-Phenylethyl)carbamoyl)nonanoylamino)phenyl)methyl)phosphonic acid **210775-30-7P**, ((4-(9-((3,5-Dimethylphenyl)carbamoyl)nonanoylamino)phenyl)methyl)phosphonic acid **210775-31-8P**, ((3-((9-(((1-Naphthyl)methyl)carbamoyl)nonanoyl)amino)phenyl)methyl)phosphonic acid **210775-32-9P**, ((4-(9-(Benzylcarbamoyl)nonanoylamino)phenyl)methyl)phosphonic acid **210775-33-0P**, ((4-(9-((4-tert-Butylphenyl)carbamoyl)nonanoylamino)phenyl)methyl)phosphonic acid **210775-34-1P**, ((4-(9-((3-(Trifluoroacetyl)phenyl)carbamoyl)nonanoylamino)phenyl)methyl)phosphonic acid **210775-35-2P**, ((4-(9-((4-(Trifluoroacetyl)phenyl)carbamoyl)nonanoylamino)phenyl)methyl)phosphonic acid **210775-36-3P**, ((4-(13-((3-(Trifluoroacetyl)phenyl)carbamoyl)tridecanoylamino)phenyl)methyl)phosphonic acid **210775-37-4P**, ((4-((13-((1-Anthracenyl)carbamoyl)tridecanoyl)amino)phenyl)methyl)phosphonic acid **210775-42-1P**, ((4-(9-((3-(Dihydroxyboryl)phenyl)carbamoyl)nonanoylamino)phenyl)methyl)phosphonic acid **210775-43-2P**, ((4-(14-((3-(Dihydroxyboryl)phenyl)carbamoyl)tetradecanoylamino)phenyl)methyl)phosphonic acid **210775-47-6P**, (2-(4-(9-((4-Phosphonomethylphenyl)carbamoyl)nonanoylamino)phenyl)ethyl)phosphonic acid **210775-48-7P**, (Difluoro(4-((9-(phenylcarbamoyl)nonanoyl)amino)phenyl)methyl)phosphonic acid **210775-49-8P**, (Ethoxy(4-((9-(phenylcarbamoyl)nonanoyl)amino)phenyl)methyl)phosphonic acid
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of mixed benzene boron and phosphorus acid derivs. as angiogenesis inhibitors)

RN 210775-03-4 CAPLUS

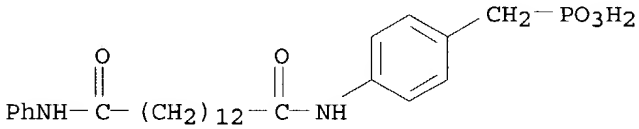
CN Phosphonic acid, [[4-[[1,10-dioxo-10-(phenylamino)decyl]amino]phenyl]methyl]- (9CI) (CA INDEX NAME)



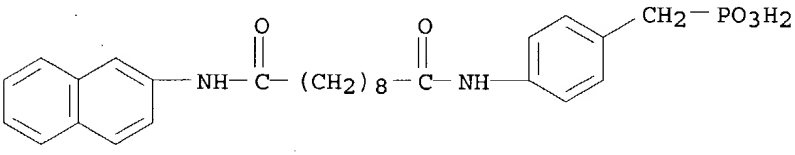
RN 210775-04-5 CAPLUS
CN Phosphonic acid, [[4-[[10-(phenylamino)decyl]amino]phenyl]methyl]- (9CI) (CA INDEX NAME)



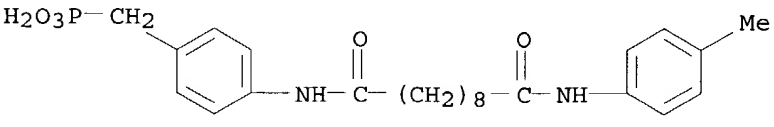
RN 210775-11-4 CAPLUS
CN Phosphonic acid, [[4-[[1,14-dioxo-14-(phenylamino)tetradecyl]amino]phenyl]methyl]- (9CI) (CA INDEX NAME)



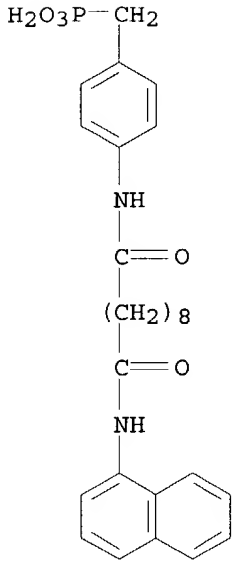
RN 210775-13-6 CAPLUS
CN Phosphonic acid, [[4-[[10-(2-naphthalenylamino)-1,10-dioxodecyl]amino]phenyl]methyl]- (9CI) (CA INDEX NAME)



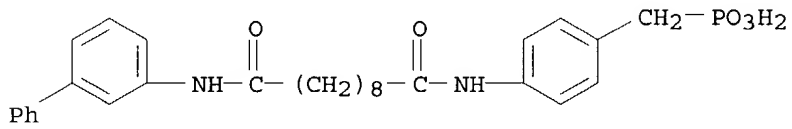
RN 210775-19-2 CAPLUS
CN Phosphonic acid, [[4-[[10-[(4-methylphenyl)amino]-1,10-dioxodecyl]amino]phenyl]methyl]- (9CI) (CA INDEX NAME)



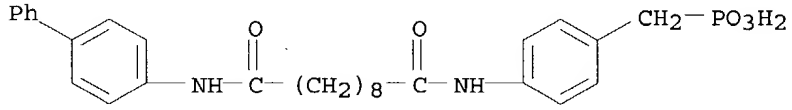
RN 210775-20-5 CAPLUS
CN Phosphonic acid, [[4-[[10-(1-naphthalenylamino)-1,10-dioxodecyl]amino]phenyl]methyl]- (9CI) (CA INDEX NAME)



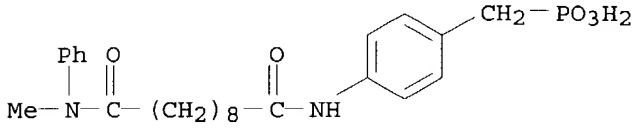
RN 210775-21-6 CAPLUS
CN Phosphonic acid, [[4-[[10-([1,1'-biphenyl]-3-ylamino)-1,10-dioxodecyl]amino]phenyl]methyl]- (9CI) (CA INDEX NAME)



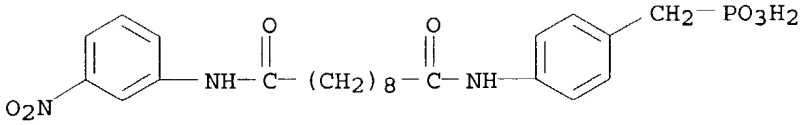
RN 210775-22-7 CAPLUS
CN Phosphonic acid, [[4-[[10-([1,1'-biphenyl]-4-ylamino)-1,10-dioxodecyl]amino]phenyl]methyl]- (9CI) (CA INDEX NAME)



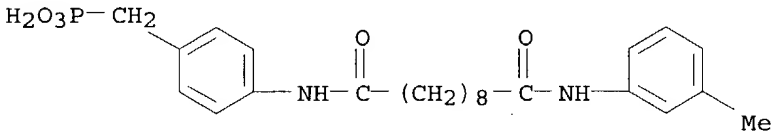
RN 210775-24-9 CAPLUS
CN Phosphonic acid, [[4-[[10-(methylphenylamino)-1,10-dioxodecyl]amino]phenyl]methyl]- (9CI) (CA INDEX NAME)



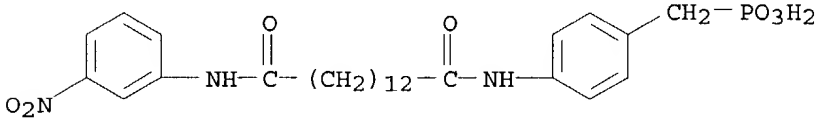
RN 210775-25-0 CAPLUS
CN Phosphonic acid, [[4-[[10-[(3-nitrophenyl)amino]-1,10-dioxodecyl]amino]phenyl]methyl]- (9CI) (CA INDEX NAME)



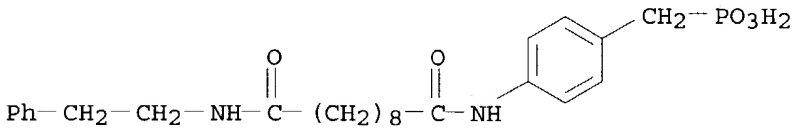
RN 210775-26-1 CAPLUS
CN Phosphonic acid, [[4-[[10-[(3-methylphenyl)amino]-1,10-dioxodecyl]amino]phenyl]methyl]- (9CI) (CA INDEX NAME)



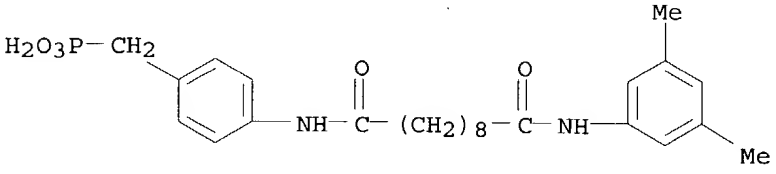
RN 210775-27-2 CAPLUS
CN Phosphonic acid, [[4-[[14-[(3-nitrophenyl)amino]-1,14-dioxotetradecyl]amino]phenyl]methyl]- (9CI) (CA INDEX NAME)



RN 210775-29-4 CAPLUS
CN Phosphonic acid, [[4-[[1,10-dioxo-10-[(2-phenylethyl)amino]decyl]amino]phenyl]methyl]- (9CI) (CA INDEX NAME)

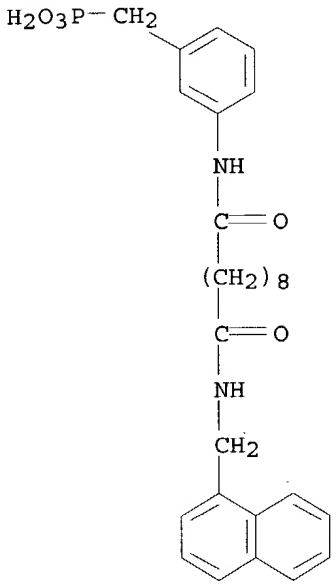


RN 210775-30-7 CAPLUS
CN Phosphonic acid, [[4-[[10-[(3,5-dimethylphenyl)amino]-1,10-dioxodecyl]amino]phenyl]methyl]- (9CI) (CA INDEX NAME)

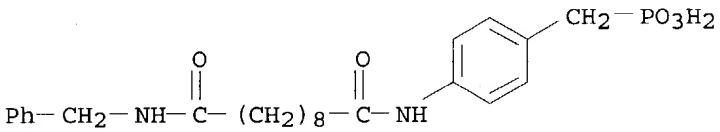


RN 210775-31-8 CAPLUS

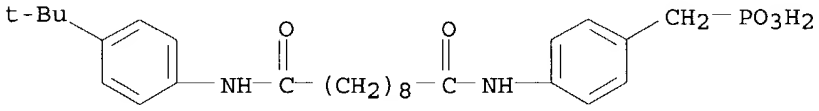
CN Phosphonic acid, [[3-[[10-[(1-naphthalenylmethyl)amino]-1,10-dioxodecyl]amino]phenyl]methyl]- (9CI) (CA INDEX NAME)



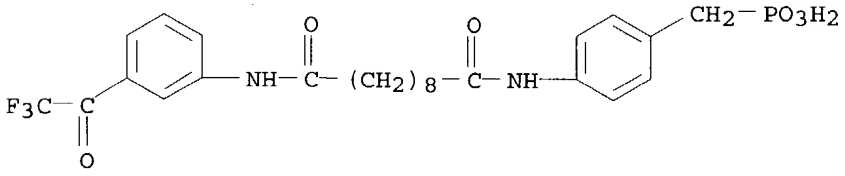
RN 210775-32-9 CAPLUS
CN Phosphonic acid, [[4-[[1,10-dioxo-10-[(phenylmethyl)amino]decyl]amino]phenyl]methyl]- (9CI) (CA INDEX NAME)



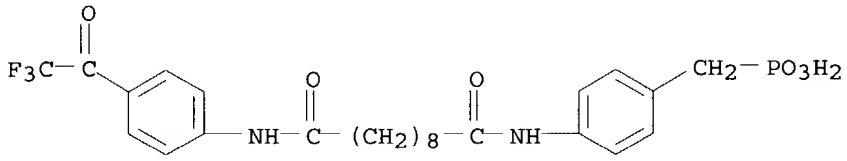
RN 210775-33-0 CAPLUS
CN Phosphonic acid, [[4-[[10-[[4-(1,1-dimethylethyl)phenyl]amino]-1,10-dioxodecyl]amino]phenyl]methyl]- (9CI) (CA INDEX NAME)



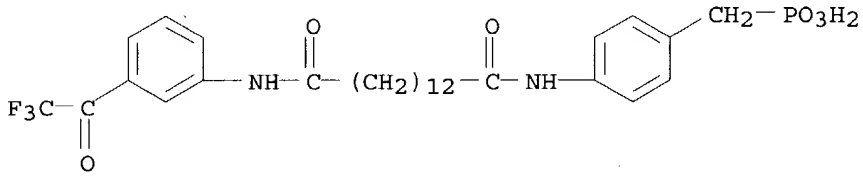
RN 210775-34-1 CAPLUS
CN Phosphonic acid, [[4-[[1,10-dioxo-10-[[3-(trifluoroacetyl)phenyl]amino]decyl]amino]phenyl]methyl]- (9CI) (CA INDEX NAME)



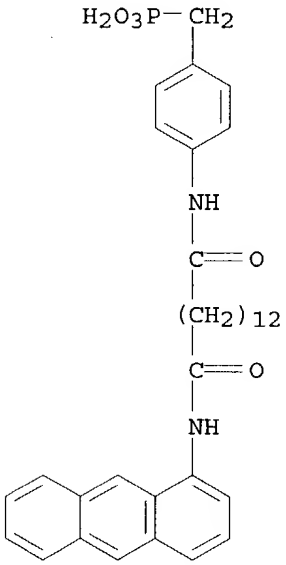
RN 210775-35-2 CAPLUS
CN Phosphonic acid, [[4-[[1,10-dioxo-10-[[4-(trifluoroacetyl)phenyl]amino]decyl]amino]phenyl]methyl]- (9CI) (CA INDEX NAME)



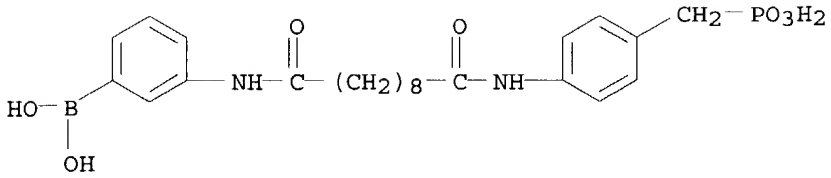
RN 210775-36-3 CAPLUS
CN Phosphonic acid, [[4-[[1,14-dioxo-14-[[3-(trifluoroacetyl)phenyl]amino]tetradecyl]amino]phenyl]methyl]- (9CI) (CA INDEX NAME)



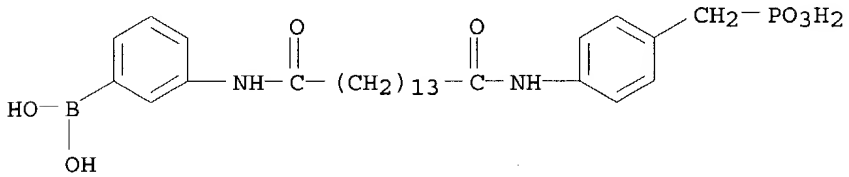
RN 210775-37-4 CAPLUS
CN Phosphonic acid, [[4-[[14-(1-anthracenylamino)-1,14-dioxotetradecyl]amino]phenyl]methyl]- (9CI) (CA INDEX NAME)



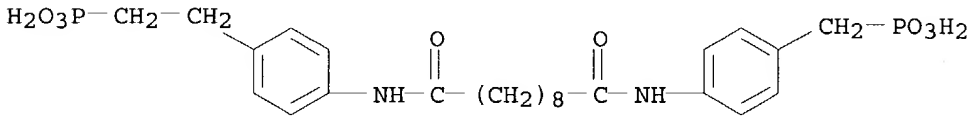
RN 210775-42-1 CAPLUS
CN Phosphonic acid, [[4-[[10-[(3-boronophenyl)amino]-1,10-dioxodecyl]amino]phenyl]methyl]- (9CI) (CA INDEX NAME)



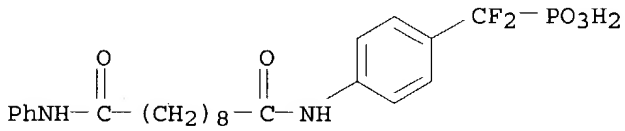
RN 210775-43-2 CAPLUS
CN Phosphonic acid, [[4-[[15-[(3-boronophenyl)amino]-1,15-dioxopentadecyl]amino]phenyl]methyl]- (9CI) (CA INDEX NAME)



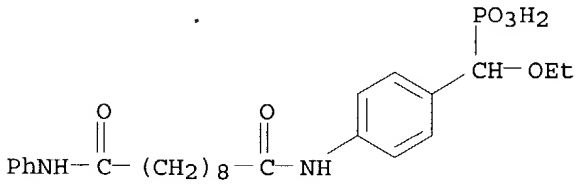
RN 210775-47-6 CAPLUS
CN Phosphonic acid, [[4-[[1,10-dioxo-10-[[4-(2-phosphonoethyl)phenyl]amino]decyl]amino]phenyl]methyl]- (9CI) (CA INDEX NAME)



RN 210775-48-7 CAPLUS
CN Phosphonic acid, [[4-[[1,10-dioxo-10-(phenylamino)decyl]amino]phenyl]difluoromethyl]- (9CI) (CA INDEX NAME)



RN 210775-49-8 CAPLUS
CN Phosphonic acid, [[4-[[1,10-dioxo-10-(phenylamino)decyl]amino]phenyl]ethoxymethyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS

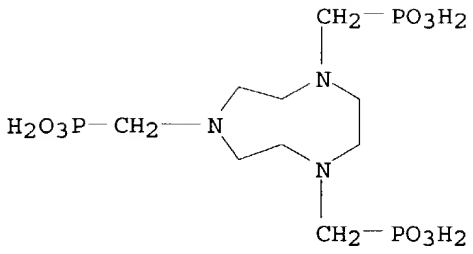
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 14 OF 18 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1997:729900 CAPLUS
DOCUMENT NUMBER: 128:70728
TITLE: IRC011, a new synthetic chelator with selective interaction with catabolic red **blood** cell iron: evaluation in hypertransfused rats with hepatocellular and reticuloendothelial radioiron probes and in iron-loaded rat heart cells in culture
AUTHOR(S): Rivkin, Gurion; Link, Gabriela; Simhon, Elliot; Cyjon, Rosa L.; Klein, Joseph Y.; Hershko, Chaim
CORPORATE SOURCE: Department of Medicine, Shaare Zedek Medical Center, Hebrew University Hadassah Medical School, Jerusalem, Israel
SOURCE: Blood (1997), 90(10), 4180-4187
CODEN: BLOOAW; ISSN: 0006-4971
PUBLISHER: Saunders
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A major consideration in the selection of new and improved iron chelators for clin. use is preferential interaction with the most toxic iron compartment. The authors describe the biol. properties of a new synthetic hexadentate iron chelator (IRC011) that is a substituted polyaza compound Unlike deferoxamine (DF), the polyaza structure of IRC011 does not contain any readily hydrolyzable covalent bonds and is anticipated to resist in vivo biotransformation. In the present studies, the ability of IRC011 to remove radioiron from iron-loaded heart cells in vitro was similar to DF, with a decrease to 20.0% and 19.7% of initial values after 24 h of incubation with 0.3 mmol/L of DF or IRC011, resp. The in vivo interaction of IRC011 with specific iron stores was studied in hypertransfused rats using selective labeling of reticuloendothelial (RE) iron stores with 59Fe-heat-denatured red **blood** cells (DRBCs) and of hepatocellular stores with 59Fe-ferritin. The pattern of radioiron excretion with IRC011 was quite different from that with DF. Although with both compds., hepatocellular iron excretion was through the bile, whereas RE iron excretion was mainly in the urine, the magnitude of these effects was quite different. After the administration of a single parenteral dose of 200 mg/kg representing a 53% higher iron-binding capacity for IRC011 compared with DF, 48-h urinary excretion of RE iron with IRC011 was 22.8% (% of total body 59Fe), but only 6.0% with DF. By contrast, the corresponding biliary excretion of hepatocellular radioiron was 14.2% with DF, but only 0.7% with IRC011. Thus, the new iron chelator IRC011 is distinguished from DF by the following features: (1) a higher affinity to Fe(III), (2) anticipated resistance to in vivo catabolism, (3) preferential interaction with RE iron derived from RBC breakdown, and (4) selective renal excretion. Because RBC breakdown is the most likely source of the toxic nontranferrin plasma iron, IRC011 may be a useful iron chelator for protecting vital organs from peroxidative damage.

IT **83834-39-3**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(IRC011 as new synthetic chelator with selective interaction with catabolic red **blood** cell iron evaluated in in hepatocellular and reticuloendothelial compartments hypertransfused rats and in heart cells)

RN 83834-39-3 CAPLUS
CN Phosphonic acid, [(hexahydro-1H-1,4,7-triazonine-1,4,7-triyl)tris(methylene)]tris- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 15 OF 18 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1992:113537 CAPLUS
DOCUMENT NUMBER: 116:113537
TITLE: Radiopharmaceutical formulations, their method of administration and process of preparation
INVENTOR(S): Simon, Jaime; Garlich, Joseph R.; Frank, R. Keith; McMillan, Kenneth
PATENT ASSIGNEE(S): Dow Chemical Co., USA
SOURCE: Eur. Pat. Appl., 20 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 462787	A1	19911227	EP 1991-305485	19910618
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
BR 9102579	A	19920121	BR 1991-2579	19910614
SK 279598	B6	19990111	SK 1991-1842	19910614
AU 9178470	A1	19911219	AU 1991-78470	19910617
AU 651112	B2	19940714		
CA 2044812	AA	19911219	CA 1991-2044812	19910617
CA 2044812	C	20021231		
FI 9102933	A	19911219	FI 1991-2933	19910617
FI 101044	B	19980415		
NO 9102345	A	19911219	NO 1991-2345	19910617
HU 57994	A2	19920128	HU 1991-2011	19910617
CN 1063615	A	19920819	CN 1991-104343	19910617
CN 1033143	B	19961030		
JP 04230224	A2	19920819	JP 1991-144735	19910617
ZA 9104615	A	19930224	ZA 1991-4615	19910617
IN 173170	A	19940226	IN 1991-MA462	19910617
IL 98536	A1	19961031	IL 1991-98536	19910617
RU 2095085	C1	19971110	RU 1991-4895658	19910617
JP 2002114712	A2	20020416	JP 2001-314293	19910617
PL 165699	B1	19950131	PL 1991-290717	19910618
ES 2073678	T3	19950816	ES 1991-305485	19910618
IN 175106	A	19950429	IN 1993-MA177	19930310
US 5762907	A	19980609	US 1993-133806	19931007
AU 9464559	A1	19940804	AU 1994-64559	19940606
AU 665911	B2	19960118		

PRIORITY APPLN. INFO.: US 1990-538871 A 19900618
IN 1991-MA462 A1 19910617
JP 1991-144735 A3 19910617

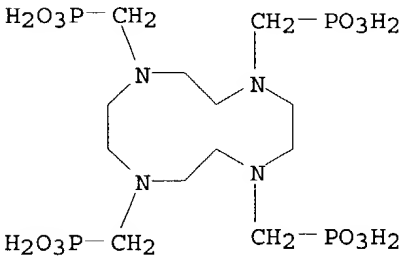
AB Radiopharmaceutical formulations comprise ≥1 radionuclide complexes with a ligand, especially, Sm153 ethylenediaminetetramethylenephosphonic acid (EDTMP) and optionally contains a divalent metal ion, e.g. Ca to minimize

the presence of free ligand to be introduced into the **blood** stream. The formulations are frozen to reduce the radiolysis, then thawed prior to use. Thus, a solution containing 0.08 M EDTMP and 3x10-4 M Sm (100 mCi Sm153/mL) was prepared and 200 μL aliquots were placed in plastic vials and frozen using a dry ice-acetone bath. A frozen vial was allowed to thaw at ambient temperature and the solution was analyzed by HPLC; the results showed only 1 radiometric peak corresponding to the desired product (no degradation product) for over a 60 h period.

IT **91987-74-5D**, radionuclide complexes
RL: BIOL (Biological study)
(radiopharmaceutical formulations containing)

RN 91987-74-5 CAPLUS

CN Phosphonic acid, [1,4,7,10-tetraazacyclododecane-1,4,7,10-tetrayltetrakis(methylene)]tetrakis- (9CI) (CA INDEX NAME)



L10 ANSWER 16 OF 18 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1988:161431 CAPLUS

DOCUMENT NUMBER: 108:161431

TITLE: Method of treating cerebral ischemia using 4-(phosphonoalkyl- or -alkenyl)piperazine-2-carboxylic acids and their salts, esters and amides

INVENTOR(S): Boast, Carl A.

PATENT ASSIGNEE(S): Ciba-Geigy Corp., USA

SOURCE: U.S., 4 pp.
CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

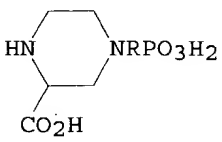
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4705781	A	19871110	US 1986-916967	19861008

PRIORITY APPLN. INFO.: US 1986-916967 19861008

GI



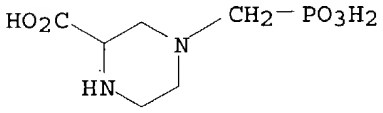
I

AB Cerebral ischemia is treated or prevented by administration of title compds. I (R = lower alkylene, lower alkenylene) or their **pharmaceutically** acceptable esters, amides, or salts. Gerbils

were injected with I (R = CH2CH2CH2) at 10 mg/kg i.p. 15 min prior or immediately after a 20 min occlusion of **blood** flow in the carotid arteries, and were subsequently dosed at 2, 4, and 6 h. The brain damage exhibited by both groups of gerbils was significantly less than in saline-treated controls, as determined by motor activity and histol. evaluation.

IT **113919-36-1**
RL: BIOL (Biological study)
(prevention by, of ischemic brain damage)

RN 113919-36-1 CAPLUS
CN 2-Piperazinecarboxylic acid, 4-(phosphonomethyl)- (9CI) (CA INDEX NAME)

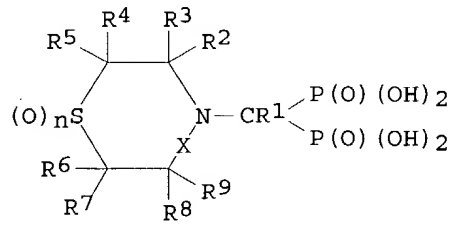


L10 ANSWER 17 OF 18 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1987:598657 CAPLUS
DOCUMENT NUMBER: 107:198657
TITLE: Novel bisphosphonic acid derivatives, a method for their production and **pharmaceutical** compositions containing them
INVENTOR(S): Binderup, Ernst Torndal; Liisberg, Sven
PATENT ASSIGNEE(S): Leo Pharmaceutical Products Ltd., Den.
SOURCE: PCT Int. Appl., 33 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 8703598	A1	19870618	WO 1986-DK132	19861210
W: DK, JP, US				
RW: BE, DE, FR, GB, IT, LU, NL, SE				
EP 248854	A1	19871216	EP 1987-900075	19861210
EP 248854	B1	19900425		
R: BE, DE, FR, GB, IT, LU, NL, SE				
JP 63501956	T2	19880804	JP 1987-500254	19861210
CA 1287350	A1	19910806	CA 1986-525118	19861211
DK 8704069	A	19870805	DK 1987-4069	19870805
DK 169678	B1	19950109		
US 4870063	A	19890926	US 1987-90980	19870810

PRIORITY APPLN. INFO.: GB 1985-30603 19851212
WO 1986-DK132 19861210

GI

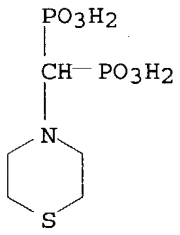


I

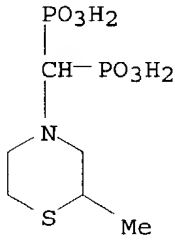
AB Title compds. I [R1-R9 = H, aryl, aralkyl, C1-10 aliphatic or alicyclic hydrocarbyl; X = (CR10R11)m; R10, R11 = R1; n = 0, 1; m = 0-2], their **pharmaceutically** acceptable salts and in vivo hydrolyzable esters are prepared and are useful for reducing bone resorption and stimulating bone alkaline phosphatase (no data). A CH2Cl2 of 26.2 g N-formylthiomorpholine was treated with (COCl)2 at 0° until gas evolution ceased. The product was treated with P(OEt)3 followed by acid hydrolysis to give (4-thiomorpholinylmethylene)bis(phosphonic acid).

IT **111072-49-2P 111072-50-5P 111072-51-6P**
111072-52-7P 111072-53-8P 111072-54-9P
111072-55-0P 111072-56-1P 111072-57-2P
111072-58-3P 111072-59-4P 111072-60-7P
111072-61-8P 111072-63-0P 111072-64-1P
111072-65-2P 111072-66-3P 111072-67-4P
111072-69-6P 111072-71-0P 111072-72-1P
111072-73-2P 111072-74-3P 111072-75-4P
111072-76-5P 111072-77-6P 111072-78-7P
111072-79-8P 111072-80-1P 111072-81-2P
111072-82-3P 111072-83-4P 111072-84-5P
111072-85-6P 111072-86-7P 111072-87-8P
111072-88-9P 111072-93-6P 111093-46-0P
111093-48-2P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, for treatment of calcium metabolic disorders)

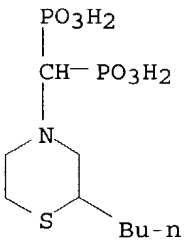
RN 111072-49-2 CAPLUS
CN Phosphonic acid, (4-thiomorpholinylmethylene)bis- (9CI) (CA INDEX NAME)



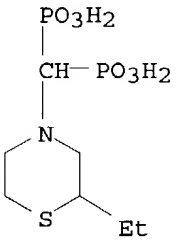
RN 111072-50-5 CAPLUS
CN Phosphonic acid, [(2-methyl-4-thiomorpholinyl)methylene]bis- (9CI) (CA INDEX NAME)



RN 111072-51-6 CAPLUS
CN Phosphonic acid, [(2-butyl-4-thiomorpholinyl)methylene]bis- (9CI) (CA INDEX NAME)



RN 111072-52-7 CAPLUS
CN Phosphonic acid, [(2-ethyl-4-thiomorpholinyl)methylene]bis- (9CI) (CA INDEX NAME)



=> d ibib abs hitstr 10-18 l10

L10 ANSWER 10 OF 18 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:117065 CAPLUS
DOCUMENT NUMBER: 132:161274
TITLE: CMP derivative sialyltransferase inhibitors, preparation, **pharmaceutical** compositions, and therapeutic use
INVENTOR(S): Schmidt, Richard R.; Schaub, Christoph; Muller, Bernd; Amann, Franz
PATENT ASSIGNEE(S): Germany
SOURCE: PCT Int. Appl., 63 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000008040	A1	20000217	WO 1999-EP5697	19990806
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9960791	A1	20000228	AU 1999-60791	19990806

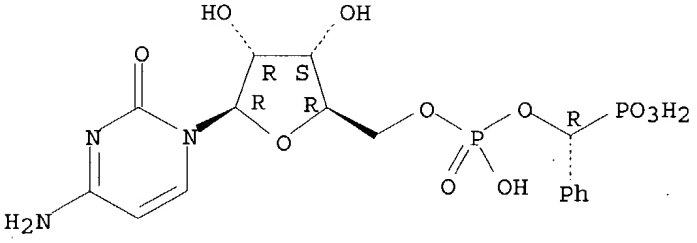
PRIORITY APPLN. INFO.: US 1998-95700P P 19980807
WO 1999-EP5697 W 19990806
OTHER SOURCE(S): MARPAT 132:161274

AB The invention provides potent inhibitors of sialyltransferases. The sialyltransferase inhibitors are useful for inhibiting the synthesis of sialylated glycosides. The sialyltransferase inhibitors find use in the modulation of biol. processes that involve sialyl glycoside-mediated cell adhesion. The compds. of the invention may be used e.g. to treat inflammation.

IT **258857-06-6P 258857-07-7P 258857-08-8P**
258857-09-9P 258857-13-5P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(CMP derivative sialyltransferase inhibitors, preparation, **pharmaceutical** compns., and therapeutic use)

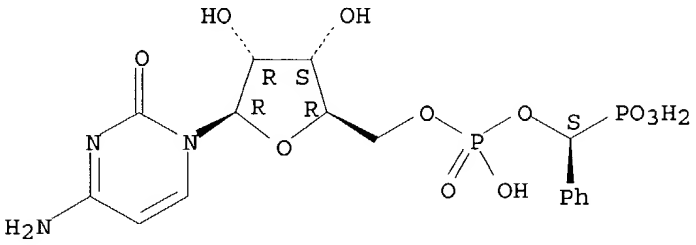
RN 258857-06-6 CAPLUS
CN 5'-Cytidylic acid, mono[(R)-phenylphosphonomethyl] ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



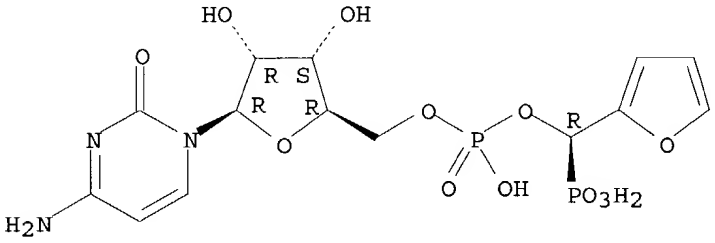
RN 258857-07-7 CAPLUS
CN 5'-Cytidylic acid, mono[(S)-phenylphosphonomethyl] ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



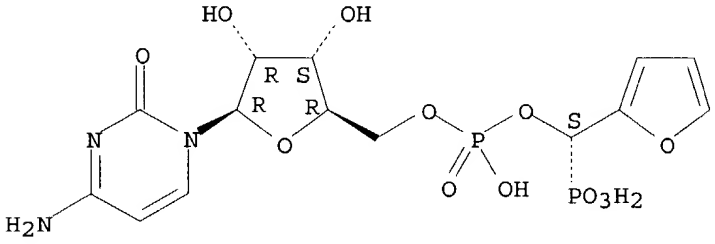
RN 258857-08-8 CAPLUS
CN 5'-Cytidylic acid, mono[(R)-2-furanylphosphonomethyl] ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



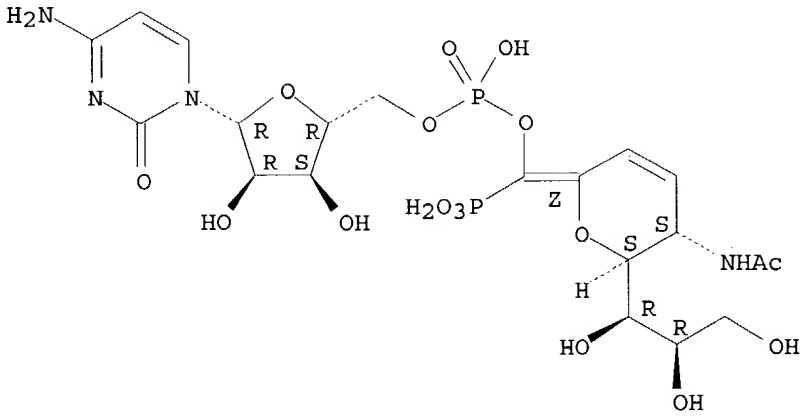
RN 258857-09-9 CAPLUS
CN 5'-Cytidylic acid, mono[(S)-2-furanylphosphonomethyl] ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



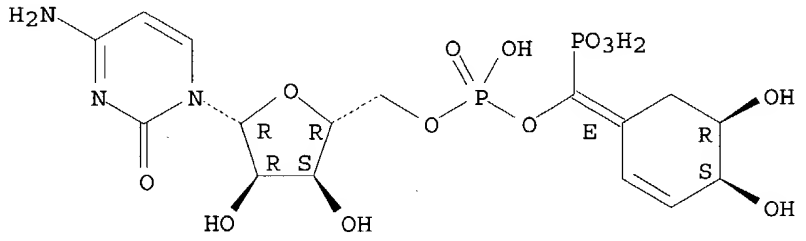
RN 258857-13-5 CAPLUS
CN 5'-Cytidylic acid, 1-ester with (1Z)-5-(acetylamino)-2,6-anhydro-3,4,5-trideoxy-1-C-phosphono-D-manno-nona-1,3-dienitol (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



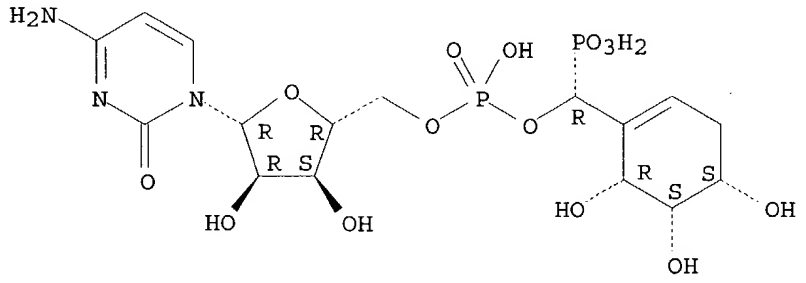
IT **258857-14-6 258860-27-4 258860-28-5**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(CMP derivative sialyltransferase inhibitors, preparation, **pharmaceutical** compns., and therapeutic use)
RN 258857-14-6 CAPLUS
CN 5'-Cytidylic acid, mono[(E)-[(4S,5R)-4,5-dihydroxy-2-cyclohexen-1-ylidene]phosphonomethyl] ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 258860-27-4 CAPLUS
CN 5'-Cytidylic acid, mono[(R)-phosphono[(4S,5S,6R)-4,5,6-trihydroxy-1-cyclohexen-1-yl]methyl] ester (9CI) (CA INDEX NAME)

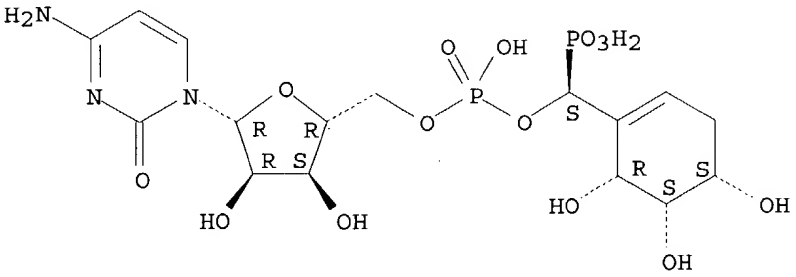
Absolute stereochemistry.



RN 258860-28-5 CAPLUS
CN 5'-Cytidylic acid, mono[(S)-phosphono[(4S,5S,6R)-4,5,6-trihydroxy-1-

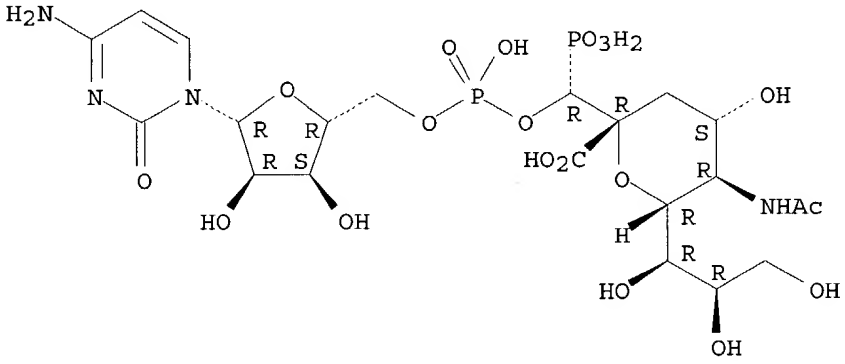
cyclohexen-1-yl]methyl] ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **258857-05-5**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(CMP derivative sialyltransferase inhibitors, preparation, **pharmaceutical** compns., and therapeutic use)
RN 258857-05-5 CAPLUS
CN D-erythro-L-manno-Nononic acid, 5-(acetylamino)-2,6-anhydro-2-C-[(R)-(5'-cytidylyloxy)phosphonomethyl]-3,5-dideoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 11 OF 18 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:34733 CAPLUS
DOCUMENT NUMBER: 132:88184
TITLE: Inhibitors of the interaction of glutamate with the AMPA and/or kainate receptor complex for treatment of demyelinating disorders
INVENTOR(S): Turski, Lechoslaw; Smith, Terence
PATENT ASSIGNEE(S): Eisai Co., Ltd, Japan
SOURCE: PCT Int. Appl., 104 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 2000001376	A2	20000113	WO 1999-GB2112	19990702
WO 2000001376	A3	20010322		
W: JP, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 1100504	A2	20010523	EP 1999-929545	19990702
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2002519373	T2	20020702	JP 2000-557823	19990702

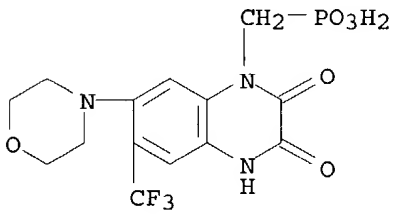
PRIORITY APPLN. INFO.:
GB 1998-14380 A 19980702
GB 1998-24393 A 19981106
WO 1999-GB2112 W 19990702

AB New therapies can be devised based upon a demonstration of the role of glutamate in the pathogenesis of demyelinating disorders. Inhibitors of the interaction of glutamate with the AMPA and/or kainate receptor complex are likely to be useful in treating demyelinating disorders and can be formulated as **pharmaceutical** compns.

IT **161605-73-8**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhibitors of interaction of glutamate with AMPA and/or kainate receptor complex for treatment of demyelinating disorders)

RN 161605-73-8 CAPLUS

CN Phosphonic acid, [[3,4-dihydro-7-(4-morpholinyl)-2,3-dioxo-6-(trifluoromethyl)-1(2H)-quinoxalinyl]methyl]- (9CI) (CA INDEX NAME)



L10 ANSWER 12 OF 18 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:96248 CAPLUS
DOCUMENT NUMBER: 130:148689
TITLE: Phosphonated agents and their antiangiogenic and antitumorigenic use
INVENTOR(S): Collins, Delwood C.; Gagliardi, Antonio R.; Nickel, Peter
PATENT ASSIGNEE(S): University of Kentucky Research Foundation, USA
SOURCE: PCT Int. Appl., 74 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

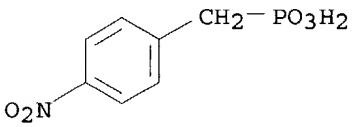
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9905148	A1	19990204	WO 1998-US15470	19980724
W: AU, CA, JP, MX				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9885915	A1	19990216	AU 1998-85915	19980724
AU 739637	B2	20011018		

EP 1019419 A1 20000719 EP 1998-937133 19980724
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI
PRIORITY APPLN. INFO.: US 1997-899996 A 19970724
WO 1998-US15470 W 19980724
OTHER SOURCE(S): MARPAT 130:148689

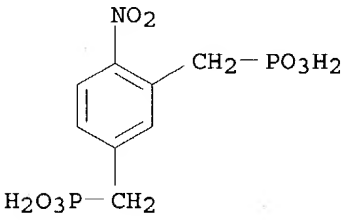
AB The present invention relates to novel phosphonic acid substituted agents and their **pharmaceutical** compns. Phosphonic acid substituted agents that are potent inhibitors of angiogenesis or tumorigenesis is defined by the following formula: (P-Yn1)m1-Q1-K-(Q2-(Yn2-P)m2)j (P = phosphonic group, phosphonic salt; Y = OCO, NR1CO, CON(R1)R2; Q1, Q2 = aryl; K = H, NHCONH, NHCSNH, NHCOR3, NHCSR3CSNH; j, n1, n2 = 0-2; m1, m2 = 1-4; R1 = H, CH2CO2H, alkyl; R2 = alkyl, aryl, alkaryl; R3 = aryl). A **pharmaceutical** composition for the treatment of angiogenesis-dependent conditions or tumors comprises an effective amount of a phosphonic acid agent and a **pharmaceutically** acceptable carrier. Some of the phosphonic acid agents were more potent inhibitors of angiogenesis in the chick chorioallantoic membrane (CAM) assay and to human microvascular endothelial cell growth than suramin.

IT **1205-62-5P 220240-22-2P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(phosphonic acid agents and their antiangiogenic and antitumorigenic use)

RN 1205-62-5 CAPLUS
CN Phosphonic acid, [(4-nitrophenyl)methyl]- (9CI) (CA INDEX NAME)



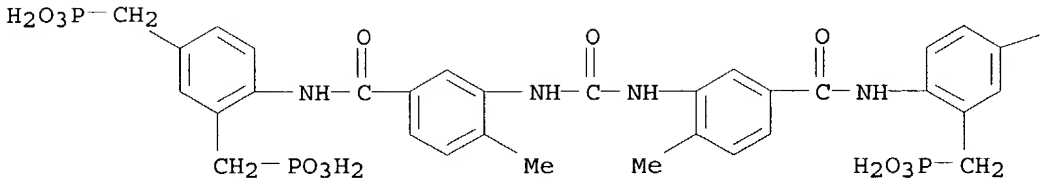
RN 220240-22-2 CAPLUS
CN Phosphonic acid, [(4-nitro-1,3-phenylene)bis(methylene)]bis- (9CI) (CA INDEX NAME)



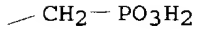
IT **220239-98-5**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(phosphonic acid agents and their antiangiogenic and antitumorigenic use)

RN 220239-98-5 CAPLUS
CN Phosphonic acid, [carbonylbis[imino(4-methyl-3,1-phenylene)carbonylimino-1,2,4-benzenetriylbis(methylene)]]tetrakis- (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 1-B



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 13 OF 18 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:509201 CAPLUS
DOCUMENT NUMBER: 129:149098
TITLE: Preparation of mixed benzene boron and phosphorus acid derivatives and **pharmaceutical** compositions useful as angiogenesis inhibitors
INVENTOR(S): Cordi, Alex; Desos, Patrice; Morris, Angela D.; Atassi, Ghanem; Pierre, Alain
PATENT ASSIGNEE(S): Adir et Cie., Fr.
SOURCE: PCT Int. Appl., 79 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

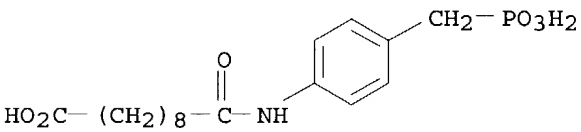
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9831689	A1	19980723	WO 1998-FR90	19980119
W: AU, BR, CA, CN, HU, JP, NO, NZ, PL, US				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
FR 2758562	A1	19980724	FR 1997-526	19970120
FR 2758562	B1	19990219		
AU 9859931	A1	19980807	AU 1998-59931	19980119
ZA 9800441	A	19980729	ZA 1998-441	19980120
PRIORITY APPLN. INFO.:			FR 1997-526	19970120
			WO 1998-FR90	19980119

OTHER SOURCE(S): CASREACT 129:149098; MARPAT 129:149098
AB The invention concerns the preparation and pharmacol. usefulness of R1R2R3C6H2A2NRaXA1XNRbA3C6H2R'1R'2R4 (R1, R2, R'1, R'2 = H, halogen, C1-6 alkyl, C1-6 alkoxy, hydroxy, nitro, trihalomethyl; or R1 and R2 (or R'1 and R'2) form together with the benzene nucleus which bears them a naphthyl or anthracenyl group; X = C:T, SO2, CH2, or X-A1-X = C(T)NHA1NHC(T) (T = O, S); A1 = C1-20 linear or branched alkylene chain with 0-6 double bonds in which ≥1 CH2 groups are replaced by O, S, CF2, phenylene, naphthylene, anthracenylene, cycloalkylene, 1,4-piperazinediyl, etc.; A2, A3 = alkylene group or single bond; R3 = H, halogen, NO2, CN, trihalomethyl, C1-6 alkyl, aryl, acyl, A4P(O)(OR6)(OR7) (A4 = single bond, alkylene), A4B(YR8)2 (Y = O, NR9; R9 = H, C1-6 alkyl); R4 = A4P(O)(OR6)(OR7), A4B(YR8)2 but R3 and R4 not both A4B(YR8)2; Ra, Rb = H, C1-6 alkyl). The invention also concerns isomers as well as additive salts to a **pharmaceutically** acceptable base. In an example

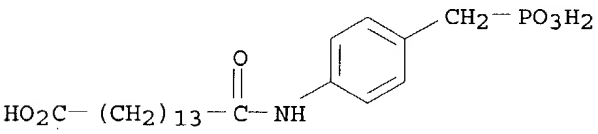
preparation, 4-(3-MeO2CC6H4NHC(O)(CH2)8C(O)NH)C6H4P(O)(OH)2 was obtained in 4 steps: 17.4 mmol of 4-H2NC6H4P(O)(OEt)2 were reacted with 17.4 mmol monomethyl sebacate, 17.4 mmol HATU and 43.5 mmol iPr2NEt in 150 mL CH2Cl2 to give MeO2C(CH2)8C(O)NH(C6H4P(O)(OEt)2-4) on workup; this intermediate was converted using KOH/H2O/MeOH to HO2C(CH2)8C(O)NH(C6H4P(O)(OEt)2-4), which was reacted with 3-H2NC6H4CO2Me in the presence of HATU and iPr2NEt in CH2Cl2 to give 4-(3-MeO2CC6H4NHC(O)(CH2)8C(O)NH)C6H4P(O)(OEt)2; finally the diester was converted to the acid using BrSiMe3 in MeCN. The above compds. are useful as angiogenesis inhibitors. Expts. are reported indicating that the compds. are powerful inhibitors of proliferation of endothelial cells and that they inhibit growth of M 5076 sarcoma in mice.

IT **210776-14-0P**, 9-((4-Phosphonomethylphenyl)carbamoyl)nonanoic acid **210776-16-2P**, 14-((4-(Phosphonomethyl)phenyl)carbamoyl)tetradecanoic acid **210776-25-3P**, Ethyl 9-((4-(ethoxy(phosphono)methyl)phenyl)carbamoyl)nonanoate **210776-27-5P**, 9-((4-(Ethoxy(phosphono)methyl)phenyl)carbamoyl)nonanoic acid
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate for preparation of mixed benzene boron and phosphorus acid derivs. as angiogenesis inhibitors)

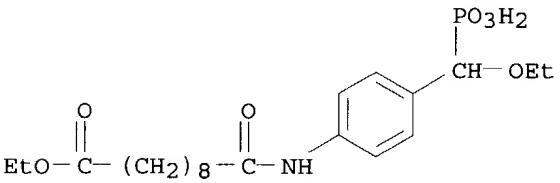
RN 210776-14-0 CAPLUS
CN Decanoic acid, 10-oxo-10-[[4-(phosphonomethyl)phenyl]amino]- (9CI) (CA INDEX NAME)



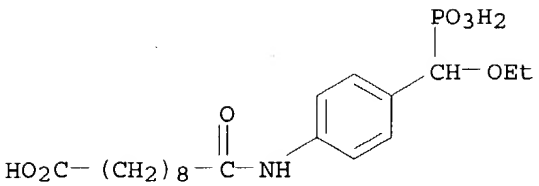
RN 210776-16-2 CAPLUS
CN Pentadecanoic acid, 15-oxo-15-[[4-(phosphonomethyl)phenyl]amino]- (9CI) (CA INDEX NAME)



RN 210776-25-3 CAPLUS
CN Decanoic acid, 10-[[4-(ethoxyphosphonomethyl)phenyl]amino]-10-oxo-, 1-ethyl ester (9CI) (CA INDEX NAME)



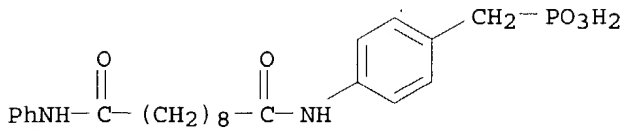
RN 210776-27-5 CAPLUS
CN Decanoic acid, 10-[[4-(ethoxyphosphonomethyl)phenyl]amino]-10-oxo- (9CI) (CA INDEX NAME)



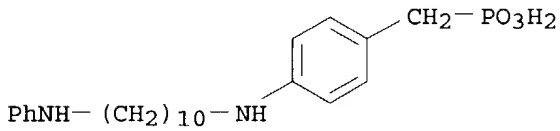
IT **210775-03-4P**, ((4-((9-(Phenylcarbamoyl)nonanoyl)amino)phenyl)methyl)phosphonic acid **210775-04-5P**, ((4-((10-(Phenylamino)decyl)amino)phenyl)methyl)phosphonic acid **210775-11-4P**, ((4-((13-(Phenylcarbamoyl)tridecanoyl)amino)phenyl)methyl)phosphonic acid **210775-13-6P**, ((4-((9-((2-Naphthyl)carbamoyl)nonanoyl)amino)phenyl)methyl)phosphonic acid **210775-19-2P**, ((4-(9-((4-Tolyl)carbamoyl)nonanoylamino)phenyl)methyl)phosphonic acid **210775-20-5P**, ((4-((9-((1-Naphthyl)carbamoyl)nonanoyl)amino)phenyl)methyl)phosphonic acid **210775-21-6P**, ((4-((9-((3-Biphenylyl)carbamoyl)nonanoyl)amino)phenyl)methyl)phosphonic acid **210775-22-7P**, ((4-((9-((4-Biphenylyl)carbamoyl)nonanoyl)amino)phenyl)methyl)phosphonic acid **210775-24-9P**, ((4-(9-(Methyl(phenyl)carbamoyl)nonanoylamino)phenyl)methyl)phosphonic acid **210775-25-0P**, ((4-(9-((3-Nitrophenyl)carbamoyl)nonanoylamino)phenyl)methyl)phosphonic acid **210775-26-1P**, ((4-(9-((3-Tolyl)carbamoyl)nonanoylamino)phenyl)methyl)phosphonic acid **210775-27-2P**, ((4-(13-((3-Nitrophenyl)carbamoyl)tridecanoylamino)phenyl)methyl)phosphonic acid **210775-29-4P**, ((4-(9-((2-Phenylethyl)carbamoyl)nonanoylamino)phenyl)methyl)phosphonic acid **210775-30-7P**, ((4-(9-((3,5-Dimethylphenyl)carbamoyl)nonanoylamino)phenyl)methyl)phosphonic acid **210775-31-8P**, ((3-((9-(((1-Naphthyl)methyl)carbamoyl)nonanoyl)amino)phenyl)methyl)phosphonic acid **210775-32-9P**, ((4-(9-(Benzylcarbamoyl)nonanoylamino)phenyl)methyl)phosphonic acid **210775-33-0P**, ((4-(9-((4-tert-Butylphenyl)carbamoyl)nonanoylamino)phenyl)methyl)phosphonic acid **210775-34-1P**, ((4-(9-((3-(Trifluoroacetyl)phenyl)carbamoyl)nonanoylamino)phenyl)methyl)phosphonic acid **210775-35-2P**, ((4-(9-((4-(Trifluoroacetyl)phenyl)carbamoyl)nonanoylamino)phenyl)methyl)phosphonic acid **210775-36-3P**, ((4-(13-((3-(Trifluoroacetyl)phenyl)carbamoyl)tridecanoylamino)phenyl)methyl)phosphonic acid **210775-37-4P**, ((4-((13-((1-Anthracenyl)carbamoyl)tridecanoyl)amino)phenyl)methyl)phosphonic acid **210775-42-1P**, ((4-(9-((3-(Dihydroxyboryl)phenyl)carbamoyl)nonanoylamino)phenyl)methyl)phosphonic acid **210775-43-2P**, ((4-(14-((3-(Dihydroxyboryl)phenyl)carbamoyl)tetradecanoylamino)phenyl)methyl)phosphonic acid **210775-47-6P**, (2-(4-(9-((4-Phosphonomethylphenyl)carbamoyl)nonanoylamino)phenyl)ethyl)phosphonic acid **210775-48-7P**, (Difluoro(4-((9-(phenylcarbamoyl)nonanoyl)amino)phenyl)methyl)phosphonic acid **210775-49-8P**, (Ethoxy(4-((9-(phenylcarbamoyl)nonanoyl)amino)phenyl)methyl)phosphonic acid
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of mixed benzene boron and phosphorus acid derivs. as angiogenesis inhibitors)

RN 210775-03-4 CAPLUS

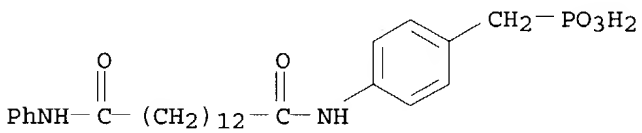
CN Phosphonic acid, [[4-[[1,10-dioxo-10-(phenylamino)decyl]amino]phenyl]methyl]- (9CI) (CA INDEX NAME)



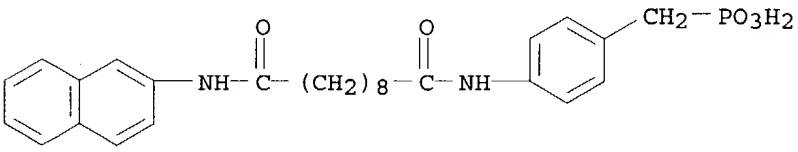
RN 210775-04-5 CAPLUS
CN Phosphonic acid, [[4-[[10-(phenylamino)decyl]amino]phenyl]methyl]- (9CI) (CA INDEX NAME)



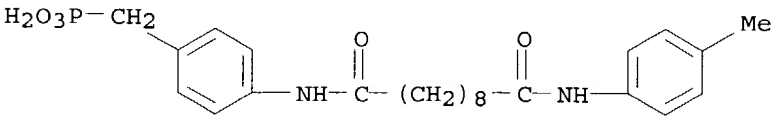
RN 210775-11-4 CAPLUS
CN Phosphonic acid, [[4-[[1,14-dioxo-14-(phenylamino)tetradecyl]amino]phenyl]methyl]- (9CI) (CA INDEX NAME)



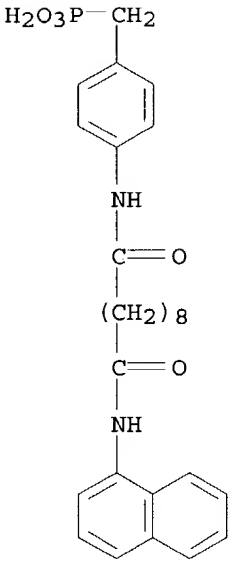
RN 210775-13-6 CAPLUS
CN Phosphonic acid, [[4-[[10-(2-naphthalenylamino)-1,10-dioxodecyl]amino]phenyl]methyl]- (9CI) (CA INDEX NAME)



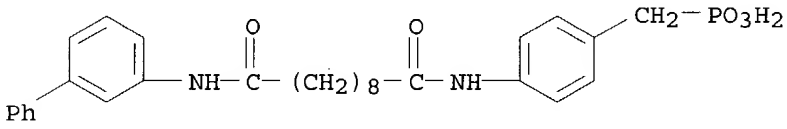
RN 210775-19-2 CAPLUS
CN Phosphonic acid, [[4-[[10-[(4-methylphenyl)amino]-1,10-dioxodecyl]amino]phenyl]methyl]- (9CI) (CA INDEX NAME)



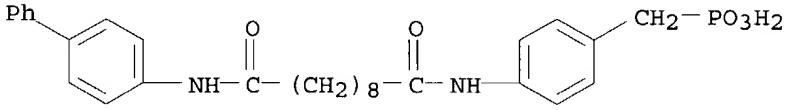
RN 210775-20-5 CAPLUS
CN Phosphonic acid, [[4-[[10-(1-naphthalenylamino)-1,10-dioxodecyl]amino]phenyl]methyl]- (9CI) (CA INDEX NAME)



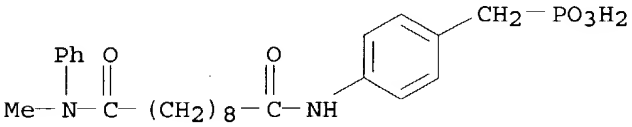
RN 210775-21-6 CAPLUS
CN Phosphonic acid, [[4-[[10-([1,1'-biphenyl]-3-ylamino)-1,10-dioxodecyl]amino]phenyl]methyl]- (9CI) (CA INDEX NAME)



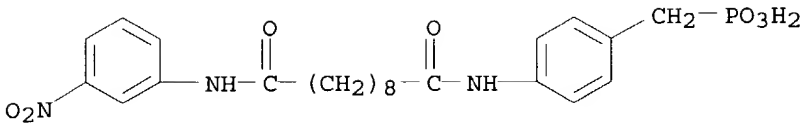
RN 210775-22-7 CAPLUS
CN Phosphonic acid, [[4-[[10-([1,1'-biphenyl]-4-ylamino)-1,10-dioxodecyl]amino]phenyl]methyl]- (9CI) (CA INDEX NAME)



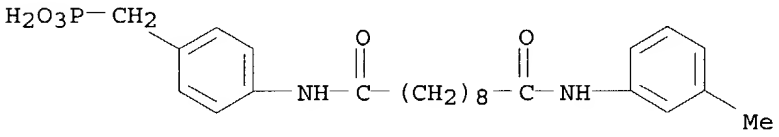
RN 210775-24-9 CAPLUS
CN Phosphonic acid, [[4-[[10-(methylphenylamino)-1,10-dioxodecyl]amino]phenyl]methyl]- (9CI) (CA INDEX NAME)



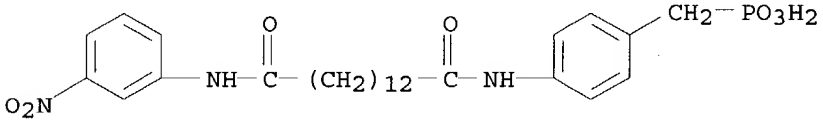
RN 210775-25-0 CAPLUS
CN Phosphonic acid, [[4-[[10-[(3-nitrophenyl)amino]-1,10-dioxodecyl]amino]phenyl]methyl]- (9CI) (CA INDEX NAME)



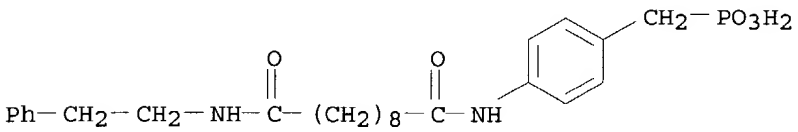
RN 210775-26-1 CAPLUS
CN Phosphonic acid, [[4-[[10-[(3-methylphenyl)amino]-1,10-dioxodecyl]amino]phenyl]methyl]- (9CI) (CA INDEX NAME)



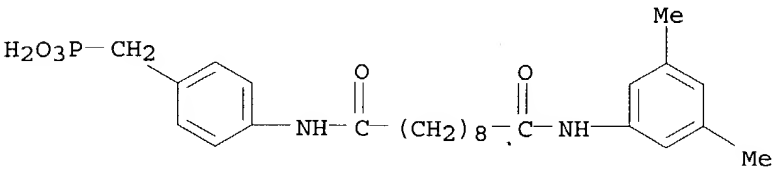
RN 210775-27-2 CAPLUS
CN Phosphonic acid, [[4-[[14-[(3-nitrophenyl)amino]-1,14-dioxotetradecyl]amino]phenyl]methyl]- (9CI) (CA INDEX NAME)



RN 210775-29-4 CAPLUS
CN Phosphonic acid, [[4-[[1,10-dioxo-10-[(2-phenylethyl)amino]decyl]amino]phenyl]methyl]- (9CI) (CA INDEX NAME)

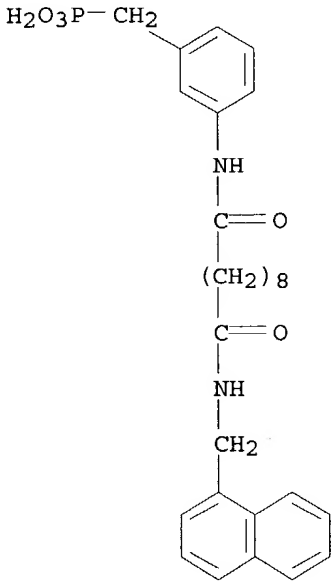


RN 210775-30-7 CAPLUS
CN Phosphonic acid, [[4-[[10-[(3,5-dimethylphenyl)amino]-1,10-dioxodecyl]amino]phenyl]methyl]- (9CI) (CA INDEX NAME)

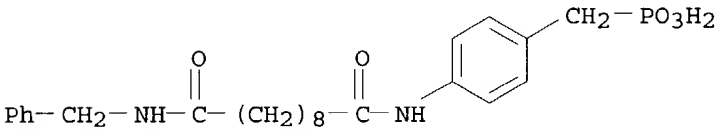


RN 210775-31-8 CAPLUS

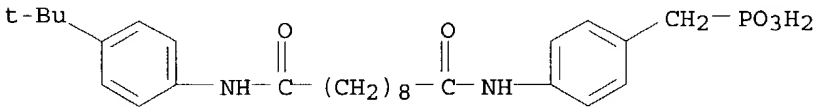
CN Phosphonic acid, [[3-[[10-[(1-naphthalenylmethyl)amino]-1,10-dioxodecyl]amino]phenyl]methyl]- (9CI) (CA INDEX NAME)



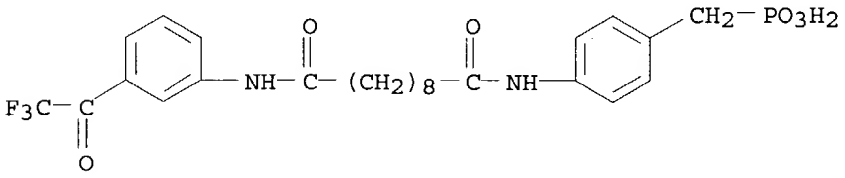
RN 210775-32-9 CAPLUS
CN Phosphonic acid, [[4-[[1,10-dioxo-10-[(phenylmethyl)amino]decyl]amino]phenyl]methyl]- (9CI) (CA INDEX NAME)



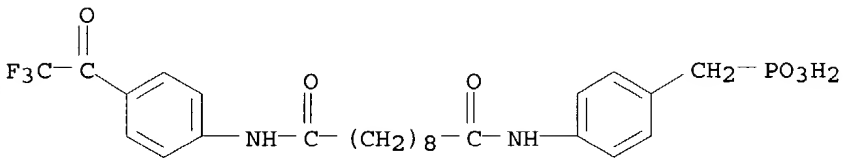
RN 210775-33-0 CAPLUS
CN Phosphonic acid, [[4-[[10-[[4-(1,1-dimethylethyl)phenyl]amino]-1,10-dioxodecyl]amino]phenyl]methyl]- (9CI) (CA INDEX NAME)



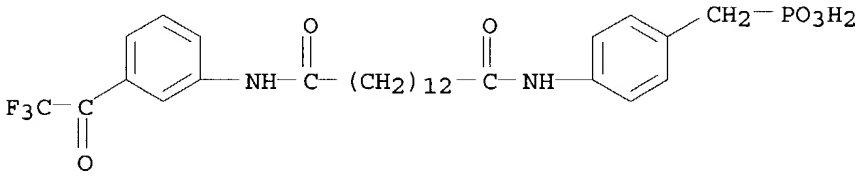
RN 210775-34-1 CAPLUS
CN Phosphonic acid, [[4-[[1,10-dioxo-10-[[3-(trifluoroacetyl)phenyl]amino]decyl]amino]phenyl]methyl]- (9CI) (CA INDEX NAME)



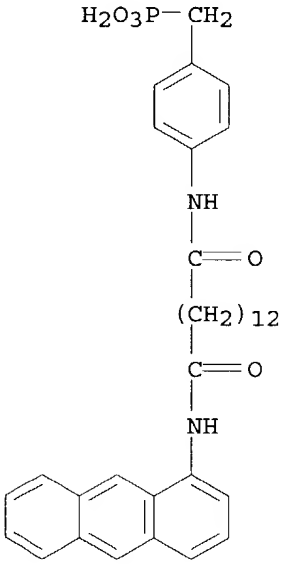
RN 210775-35-2 CAPLUS
CN Phosphonic acid, [[4-[[1,10-dioxo-10-[[4-(trifluoroacetyl)phenyl]amino]dec
yl]amino]phenyl]methyl]- (9CI) (CA INDEX NAME)



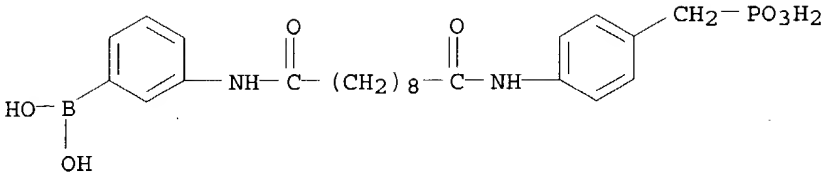
RN 210775-36-3 CAPLUS
CN Phosphonic acid, [[4-[[1,14-dioxo-14-[[3-(trifluoroacetyl)phenyl]amino]tet
radecyl]amino]phenyl]methyl]- (9CI) (CA INDEX NAME)



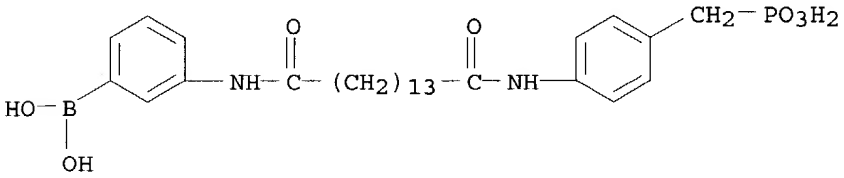
RN 210775-37-4 CAPLUS
CN Phosphonic acid, [[4-[[14-(1-anthracenylamino)-1,14-
dioxotetradecyl]amino]phenyl]methyl]- (9CI) (CA INDEX NAME)



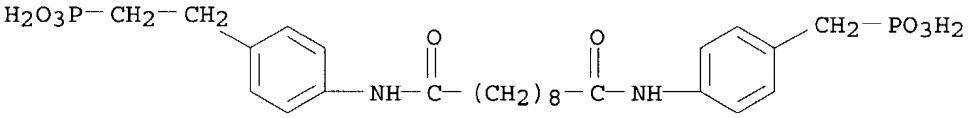
RN 210775-42-1 CAPLUS
CN Phosphonic acid, [[4-[[10-[(3-boronophenyl)amino]-1,10-
dioxodecyl]amino]phenyl]methyl]- (9CI) (CA INDEX NAME)



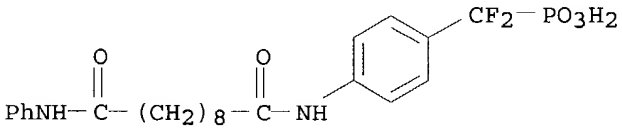
RN 210775-43-2 CAPLUS
CN Phosphonic acid, [[4-[[15-[(3-boronophenyl)amino]-1,15-dioxopentadecyl]amino]phenyl]methyl]- (9CI) (CA INDEX NAME)



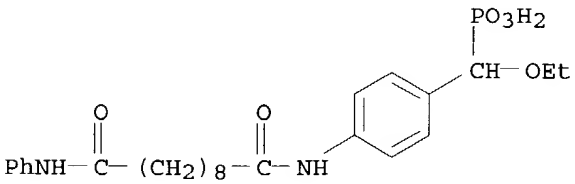
RN 210775-47-6 CAPLUS
CN Phosphonic acid, [[4-[[1,10-dioxo-10-[[4-(2-phosphonoethyl)phenyl]amino]decyl]amino]phenyl]methyl]- (9CI) (CA INDEX NAME)



RN 210775-48-7 CAPLUS
CN Phosphonic acid, [[4-[[1,10-dioxo-10-(phenylamino)decyl]amino]phenyl]difluoromethyl]- (9CI) (CA INDEX NAME)



RN 210775-49-8 CAPLUS
CN Phosphonic acid, [[4-[[1,10-dioxo-10-(phenylamino)decyl]amino]phenyl]ethoxymethyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS

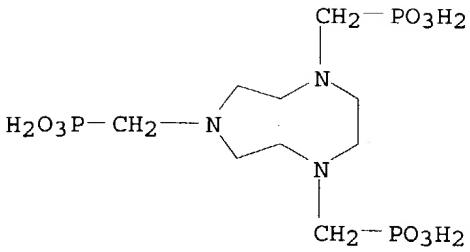
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 14 OF 18 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1997:729900 CAPLUS
DOCUMENT NUMBER: 128:70728
TITLE: IRC011, a new synthetic chelator with selective interaction with catabolic red **blood** cell iron: evaluation in hypertransfused rats with hepatocellular and reticuloendothelial radioiron probes and in iron-loaded rat heart cells in culture
AUTHOR(S): Rivkin, Gurion; Link, Gabriela; Simhon, Elliot; Cyjon, Rosa L.; Klein, Joseph Y.; Hershko, Chaim
CORPORATE SOURCE: Department of Medicine, Shaare Zedek Medical Center, Hebrew University Hadassah Medical School, Jerusalem, Israel
SOURCE: Blood (1997), 90(10), 4180-4187
CODEN: BLOOAW; ISSN: 0006-4971
PUBLISHER: Saunders
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A major consideration in the selection of new and improved iron chelators for clin. use is preferential interaction with the most toxic iron compartment. The authors describe the biol. properties of a new synthetic hexadentate iron chelator (IRC011) that is a substituted polyaza compound Unlike deferoxamine (DF), the polyaza structure of IRC011 does not contain any readily hydrolyzable covalent bonds and is anticipated to resist in vivo biotransformation. In the present studies, the ability of IRC011 to remove radioiron from iron-loaded heart cells in vitro was similar to DF, with a decrease to 20.0% and 19.7% of initial values after 24 h of incubation with 0.3 mmol/L of DF or IRC011, resp. The in vivo interaction of IRC011 with specific iron stores was studied in hypertransfused rats using selective labeling of reticuloendothelial (RE) iron stores with 59Fe-heat-denatured red **blood** cells (DRBCs) and of hepatocellular stores with 59Fe-ferritin. The pattern of radioiron excretion with IRC011 was quite different from that with DF. Although with both compds., hepatocellular iron excretion was through the bile, whereas RE iron excretion was mainly in the urine, the magnitude of these effects was quite different. After the administration of a single parenteral dose of 200 mg/kg representing a 53% higher iron-binding capacity for IRC011 compared with DF, 48-h urinary excretion of RE iron with IRC011 was 22.8% (% of total body 59Fe), but only 6.0% with DF. By contrast, the corresponding biliary excretion of hepatocellular radioiron was 14.2% with DF, but only 0.7% with IRC011. Thus, the new iron chelator IRC011 is distinguished from DF by the following features: (1) a higher affinity to Fe(III), (2) anticipated resistance to in vivo catabolism, (3) preferential interaction with RE iron derived from RBC breakdown, and (4) selective renal excretion. Because RBC breakdown is the most likely source of the toxic nontranferrin plasma iron, IRC011 may be a useful iron chelator for protecting vital organs from peroxidative damage.

IT **83834-39-3**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(IRC011 as new synthetic chelator with selective interaction with catabolic red **blood** cell iron evaluated in in hepatocellular and reticuloendothelial compartments hypertransfused rats and in heart cells)

RN 83834-39-3 CAPLUS
CN Phosphonic acid, [(hexahydro-1H-1,4,7-triazonine-1,4,7-triyl)tris(methylene)]tris- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 15 OF 18 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1992:113537 CAPLUS
DOCUMENT NUMBER: 116:113537
TITLE: Radiopharmaceutical formulations, their method of administration and process of preparation
INVENTOR(S): Simon, Jaime; Garlich, Joseph R.; Frank, R. Keith; McMillan, Kenneth
PATENT ASSIGNEE(S): Dow Chemical Co., USA
SOURCE: Eur. Pat. Appl., 20 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 462787	A1	19911227	EP 1991-305485	19910618
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
BR 9102579	A	19920121	BR 1991-2579	19910614
SK 279598	B6	19990111	SK 1991-1842	19910614
AU 9178470	A1	19911219	AU 1991-78470	19910617
AU 651112	B2	19940714		
CA 2044812	AA	19911219	CA 1991-2044812	19910617
CA 2044812	C	20021231		
FI 9102933	A	19911219	FI 1991-2933	19910617
FI 101044	B	19980415		
NO 9102345	A	19911219	NO 1991-2345	19910617
HU 57994	A2	19920128	HU 1991-2011	19910617
CN 1063615	A	19920819	CN 1991-104343	19910617
CN 1033143	B	19961030		
JP 04230224	A2	19920819	JP 1991-144735	19910617
ZA 9104615	A	19930224	ZA 1991-4615	19910617
IN 173170	A	19940226	IN 1991-MA462	19910617
IL 98536	A1	19961031	IL 1991-98536	19910617
RU 2095085	C1	19971110	RU 1991-4895658	19910617
JP 2002114712	A2	20020416	JP 2001-314293	19910617
PL 165699	B1	19950131	PL 1991-290717	19910618
ES 2073678	T3	19950816	ES 1991-305485	19910618
IN 175106	A	19950429	IN 1993-MA177	19930310
US 5762907	A	19980609	US 1993-133806	19931007
AU 9464559	A1	19940804	AU 1994-64559	19940606
AU 665911	B2	19960118		

PRIORITY APPLN. INFO.: US 1990-538871 A 19900618
IN 1991-MA462 A1 19910617
JP 1991-144735 A3 19910617

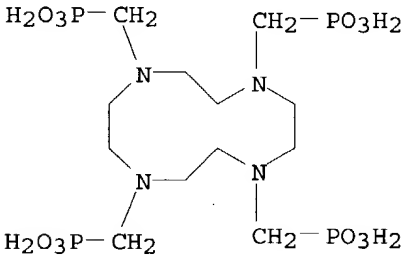
AB Radiopharmaceutical formulations comprise ≥1 radionuclide complexes with a ligand, especially, Sm153 ethylenediaminetetramethylenephosphonic acid (EDTMP) and optionally contains a divalent metal ion, e.g. Ca to minimize

the presence of free ligand to be introduced into the **blood** stream. The formulations are frozen to reduce the radiolysis, then thawed prior to use. Thus, a solution containing 0.08 M EDTMP and 3x10-4 M Sm (100 mCi
Sm153/mL) was prepared and 200 μL aliquots were placed in plastic vials and frozen using a dry ice-acetone bath. A frozen vial was allowed to thaw at ambient temperature and the solution was analyzed by HPLC; the results showed only 1 radiometric peak corresponding to the desired product (no degradation product) for over a 60 h period.

IT **91987-74-5D**, radionuclide complexes
RL: BIOL (Biological study)
(radiopharmaceutical formulations containing)

RN 91987-74-5 CAPLUS

CN Phosphonic acid, [1,4,7,10-tetraazacyclododecane-1,4,7,10-tetrayltetrakis(methylene)]tetrakis- (9CI) (CA INDEX NAME)



L10 ANSWER 16 OF 18 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1988:161431 CAPLUS

DOCUMENT NUMBER: 108:161431

TITLE: Method of treating cerebral ischemia using 4-(phosphonoalkyl- or -alkenyl)piperazine-2-carboxylic acids and their salts, esters and amides

INVENTOR(S): Boast, Carl A.

PATENT ASSIGNEE(S): Ciba-Geigy Corp., USA

SOURCE: U.S., 4 pp.
CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

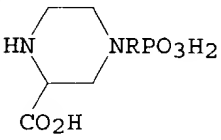
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4705781	A	19871110	US 1986-916967	19861008

PRIORITY APPLN. INFO.: US 1986-916967 19861008

GI



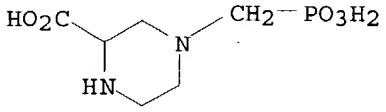
I

AB Cerebral ischemia is treated or prevented by administration of title compds. I (R = lower alkylene, lower alkenylene) or their **pharmaceutically** acceptable esters, amides, or salts. Gerbils

were injected with I (R = CH2CH2CH2) at 10 mg/kg i.p. 15 min prior or immediately after a 20 min occlusion of **blood** flow in the carotid arteries, and were subsequently dosed at 2, 4, and 6 h. The brain damage exhibited by both groups of gerbils was significantly less than in saline-treated controls, as determined by motor activity and histol. evaluation.

IT **113919-36-1**
RL: BIOL (Biological study)
(prevention by, of ischemic brain damage)

RN 113919-36-1 CAPLUS
CN 2-Piperazinecarboxylic acid, 4-(phosphonomethyl)- (9CI) (CA INDEX NAME)

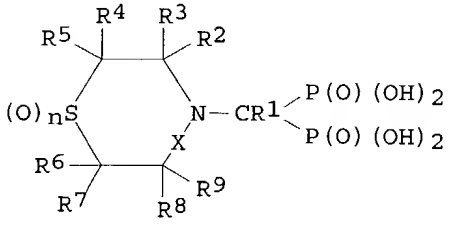


L10 ANSWER 17 OF 18 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1987:598657 CAPLUS
DOCUMENT NUMBER: 107:198657
TITLE: Novel bisphosphonic acid derivatives, a method for their production and **pharmaceutical** compositions containing them
INVENTOR(S): Binderup, Ernst Torndal; Liisberg, Sven
PATENT ASSIGNEE(S): Leo Pharmaceutical Products Ltd., Den.
SOURCE: PCT Int. Appl., 33 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 8703598	A1	19870618	WO 1986-DK132	19861210
W: DK, JP, US				
RW: BE, DE, FR, GB, IT, LU, NL, SE				
EP 248854	A1	19871216	EP 1987-900075	19861210
EP 248854	B1	19900425		
R: BE, DE, FR, GB, IT, LU, NL, SE				
JP 63501956	T2	19880804	JP 1987-500254	19861210
CA 1287350	A1	19910806	CA 1986-525118	19861211
DK 8704069	A	19870805	DK 1987-4069	19870805
DK 169678	B1	19950109		
US 4870063	A	19890926	US 1987-90980	19870810

PRIORITY APPLN. INFO.: GB 1985-30603 19851212
WO 1986-DK132 19861210

GI

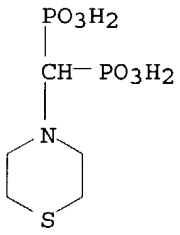


I

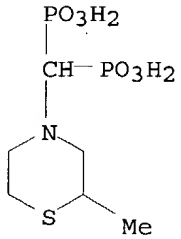
AB Title compds. I [R1-R9 = H, aryl, aralkyl, C1-10 aliphatic or alicyclic hydrocarbyl; X = (CR10R11)m; R10, R11 = R1; n = 0, 1; m = 0-2], their **pharmaceutically** acceptable salts and in vivo hydrolyzable esters are prepared and are useful for reducing bone resorption and stimulating bone alkaline phosphatase (no data). A CH2Cl2 of 26.2 g N-formylthiomorpholine was treated with (COCl)2 at 0° until gas evolution ceased. The product was treated with P(OEt)3 followed by acid hydrolysis to give (4-thiomorpholinylmethylene)bis(phosphonic acid).

IT **111072-49-2P 111072-50-5P 111072-51-6P**
111072-52-7P 111072-53-8P 111072-54-9P
111072-55-0P 111072-56-1P 111072-57-2P
111072-58-3P 111072-59-4P 111072-60-7P
111072-61-8P 111072-63-0P 111072-64-1P
111072-65-2P 111072-66-3P 111072-67-4P
111072-69-6P 111072-71-0P 111072-72-1P
111072-73-2P 111072-74-3P 111072-75-4P
111072-76-5P 111072-77-6P 111072-78-7P
111072-79-8P 111072-80-1P 111072-81-2P
111072-82-3P 111072-83-4P 111072-84-5P
111072-85-6P 111072-86-7P 111072-87-8P
111072-88-9P 111072-93-6P 111093-46-0P
111093-48-2P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, for treatment of calcium metabolic disorders)

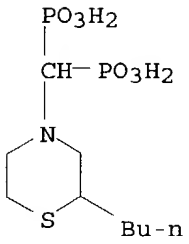
RN 111072-49-2 CAPLUS
CN Phosphonic acid, (4-thiomorpholinylmethylene)bis- (9CI) (CA INDEX NAME)



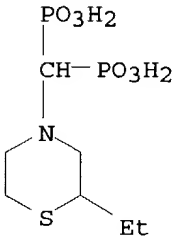
RN 111072-50-5 CAPLUS
CN Phosphonic acid, [(2-methyl-4-thiomorpholinyl)methylene]bis- (9CI) (CA INDEX NAME)



RN 111072-51-6 CAPLUS
CN Phosphonic acid, [(2-butyl-4-thiomorpholinyl)methylene]bis- (9CI) (CA INDEX NAME)



RN 111072-52-7 CAPLUS
CN Phosphonic acid, [(2-ethyl-4-thiomorpholinyl)methylene]bis- (9CI) (CA INDEX NAME)



L10 ANSWER 18 OF 18 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1982:218031 CAPLUS
DOCUMENT NUMBER: 96:218031
TITLE: Diphosphonate derivatives and **pharmaceutical** compositions containing them
INVENTOR(S): Bentzen, Craig L.; Nguyen Lan Mong; Niesor, Eric
PATENT ASSIGNEE(S): Symphar S. A., Switz.
SOURCE: Brit. UK Pat. Appl., 25 pp.
CODEN: BAXXDU
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

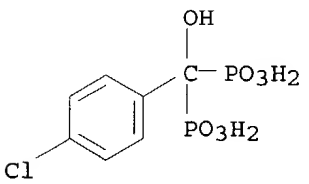
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
GB 2079285	A	19820120	GB 1980-22463	19800709
GB 2079285	B2	19840523		
US 4416877	A	19831122	US 1981-310314	19811009

PRIORITY APPLN. INFO.:
GB 1979-4992 19790213
GB 1979-33157 19790925
US 1980-114423 19800122
GB 1980-22463 19800709

AB R2O3POmCR1XPO3R22 [X = H, OH, OAc, NH2; R, R2 = H, Me, Et, Bu; m = 0, 1; R1 = Me3C, YC6H4, YC6H4OCMe2, p-(YC6H4CO)C6H4, YC6H4(CH2)n (n = 1-6), YC6H4O(CH2)n (n = 1-6), (Y = H, Me, OMe, halo)] were prepared For example, reaction of di-Me phosphite with di-Me p-chlorobenzoylphosphonate in the presence of Bu2NH gave a 92% yield of p-ClC6H4C(OH)(PO3Me2)2 (I). These diphosphonate derivs. affect lipids and lipid metabolism Thus, they act on lipid metabolism in normal rats by decreasing serum free fatty acids, decreasing triglycerides, and increasing phospholipids. In high fat high cholesterol fed rats, the diphosphonate derivs. decrease and remove significantly liver and aorta lipids, especially cholesterol. Also, the acid and salt forms of I decrease serum Ca. Some of these diphosphonates also possess hypoglycemic and antiatherogenic properties.

IT **59216-73-8P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and effects on serum calcium)

RN 59216-73-8 CAPLUS
CN Phosphonic acid, [(4-chlorophenyl)hydroxymethylene]bis- (9CI) (CA INDEX NAME)



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L18 NOT FOUND
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L10 ANSWER 18 OF 18 CAPLUS COPYRIGHT 2004 ACS on STN
IT **Blood** serum
(calcium of, effect of diphosphonates on

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L3                STRUCTURE UPLOADED
L4             50 S L3
L5                STRUCTURE UPLOADED
L6             50 S L5
L7           6573 S L5 FULL
L8           5741 S L7 NOT M/ELS

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L10            18 S L9 AND (BLOOD OR THROMBO?)
L11             0 S L10 AND COAGUL?

=> d his

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L7           6573 S L5 FULL
L8           5741 S L7 NOT M/ELS

     FILE 'CAPLUS' ENTERED AT 14:58:13 ON 03 MAY 2004
L9            172 S L8 AND PHARMACEUT?
L10            18 S L9 AND (BLOOD OR THROMBO?)
L11             0 S L10 AND COAGUL?

=> s l9 and (thrombo? or blood clot? or blood coagulat?)
          66936 THROMBO?
        1131789 BLOOD
           1163 BLOODS
        1131904 BLOOD
                  (BLOOD OR BLOODS)
          71610 CLOT?
           7255 BLOOD CLOT?
                  (BLOOD(W)CLOT?)
        1131789 BLOOD
           1163 BLOODS
        1131904 BLOOD
                  (BLOOD OR BLOODS)
         116668 COAGULAT?
          41054 BLOOD COAGULAT?
                  (BLOOD(W)COAGULAT?)
L12             2 L9 AND (THROMBO? OR BLOOD CLOT? OR BLOOD COAGULAT?)

=> d ibib abs hitstr 1-2

L12  ANSWER 1 OF 2  CAPLUS  COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER:         2003:836762  CAPLUS
DOCUMENT NUMBER:          139:350474
TITLE:                    Preparation and compositions of nitrosothio
                          (hetero)cyclic nitric oxide donors
INVENTOR(S):              Fang, Xinqin; Garvey, David S.; Gaston, Ricky D.; Lin,
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Chia-en; Ranatunga, Ramani R.; Richardson, Stewart K.; Wang, Tiansheng; Wang, Weiheng; Wey, Shiow-jyi
PATENT ASSIGNEE(S): Nitromed, Inc., USA
SOURCE: PCT Int. Appl., 138 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003086282	A2	20031023	WO 2003-US10562	20030407
US 2003203915	A1	20031030	US 2003-407420	20030407

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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2002-369873P P 20020405
OTHER SOURCE(S): MARPAT 139:350474
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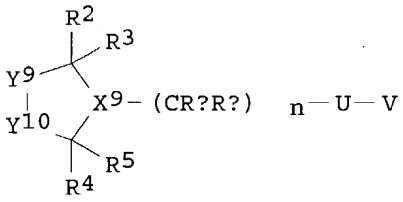

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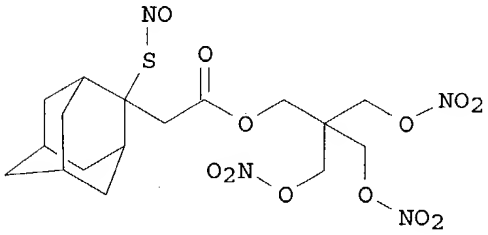


II

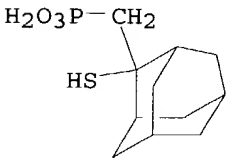
AB Title compds. I [wherein U = O, S, or NRaRi; V = NO or NO2; X9 = CR10 or N; Y9 = CR6R7, NRi, NR25, NRiCR6R7, CR6R7NRi, CR2R3CR6R7, or CR6R7CR2R3; Y10 = CR8R9 or CR8R9CR17R18; R2-R9, R17, and R18 = independently H or alkyl; or R2R3, R4R5, R6R7, or R8R9 = independently oxo; or R4 and R7 together with the C's to which they are attached = cycloalkyl; or CR6R7 = cycloalkyl; R6 and R9 taken together with the C's to which they are attached = (bridged)cycloalkyl, heterocyclyl, or aryl with the proviso that R7 and R8 are not present; R4 and R25 taken together with the C and N to which they are attached = heterocyclyl; Ra = lone pair of electrons, H, or (aryl)alkyl; Re and Rf = independently H, halo, OH, or (un)substituted (cyclo)alkyl, heterocyclyl, alkoxy, amino, aryl, etc.; or CReRf = heterocyclyl or (bridged) cycloalkyl; Ri = H or (un)substituted alkyl,

aryl, carboxamido, sulfonamido, etc.; n = 0-3; and **pharmaceutically** acceptable salts thereof] were prepared as novel nitric oxide donors for use in compns. comprising at least one nitric oxide donor and optionally at least one therapeutic agent. The nitric oxide donors donate, transfer or release nitric oxide, and/or elevate endogenous levels of endothelium-derived relaxing factor, and/or stimulate endogenous synthesis of nitric oxide and/or are substrates for nitric oxide synthase and are capable of releasing nitric oxide or indirectly delivering or transferring nitric oxide to targeted sites under physiol. conditions (no data). For example, 2-[2-(nitrosothio)adamantan-2-yl]acetic acid was esterified with 3-nitrooxy-2,2-bis(nitrooxymethyl)propan-1-ol in the presence of 1-[3-(dimethylamino)propyl]-3-ethylcarbodiimide•HCl and 4-dimethylaminopyridine in CH_2Cl_2 to give II (18%). The latter inhibited proliferation of human coronary artery smooth muscle cells with IC50 of 5 μM. In general, the nitrosylated compds. tested in this assay inhibited proliferation of vascular smooth muscle cells, while the corresponding non-nitrosylated derivs. showed no inhibition, slight inhibition, or exhibited much higher IC50 values. Thus, the invention provides methods for treating cardiovascular diseases, for the inhibition of platelet aggregation and platelet adhesion caused by the exposure of blood to a medical device, for treating pathol. conditions resulting from abnormal cell proliferation, transplantation rejections, autoimmune, inflammatory, proliferative, hyperproliferative, vascular diseases, for reducing scar tissue or for inhibiting wound contraction, particularly the prophylactic and/or therapeutic treatment of restenosis (no data). The invention also provides methods for treating inflammation, pain, fever, gastrointestinal disorders, respiratory disorders, and sexual dysfunctions (no data). In addition, the invention provides novel compns. and kits comprising at least one nitric oxide donor and/or at least one therapeutic agent.

IT **618113-20-5P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation and compns. of nitrosothio (hetero)cyclic nitric oxide donors for treatment of cardiovascular, proliferative, inflammatory, and autoimmune disorders and other conditions)

RN 618113-20-5 CAPLUS

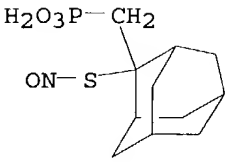
CN Phosphonic acid, [(2-mercaptotricyclo[3.3.1.13,7]dec-2-yl)methyl]- (9CI) (CA INDEX NAME)



IT **618113-19-2P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(nitric oxide donor; preparation and compns. of nitrosothio (hetero)cyclic nitric oxide donors for treatment of cardiovascular, proliferative, inflammatory, and autoimmune disorders and other conditions)

RN 618113-19-2 CAPLUS

CN Thionitrous acid (HNOS), S-[2-(phosphonomethyl)tricyclo[3.3.1.13,7]dec-2-yl] ester (9CI) (CA INDEX NAME)

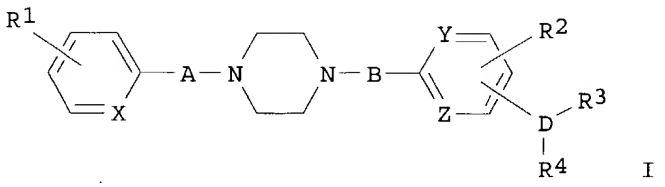


L12 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:777592 CAPLUS
DOCUMENT NUMBER: 139:292270
TITLE: Substituted piperazine antithrombotic PAI-1 (plasminogen activator inhibitor-1) inhibitors, and their preparation, **pharmaceutical** compositions, and use in the treatment of **thrombotic** diseases.
INVENTOR(S): Chou, Yuo-Ling; Ghannam, Ameen; Kochanny, Monica J.; Lee, Wheeseong; Lu, Shou-Fu; Shaw, Kenneth J.; Ye, Bin; Zhao, Zuchun
PATENT ASSIGNEE(S): Schering Aktiengesellschaft, Germany
SOURCE: PCT Int. Appl., 61 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003080060	A1	20031002	WO 2003-US7508	20030313

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2002-365988P P 20020320
OTHER SOURCE(S): MARPAT 139:292270
GI



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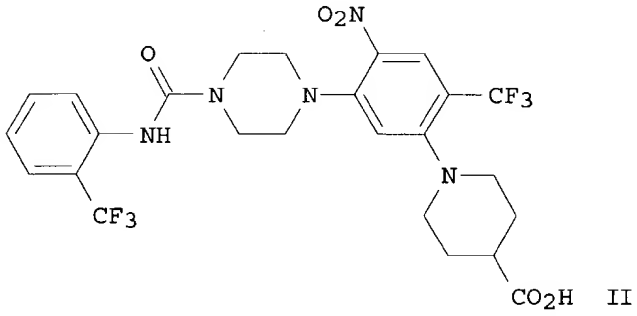


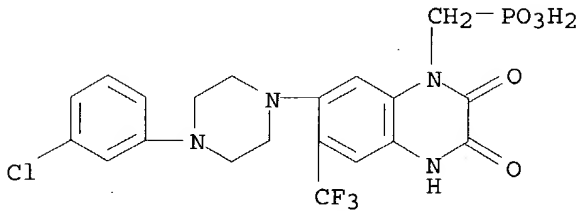
II

AB The invention is directed to substituted piperazine compds. I and their **pharmaceutically** acceptable salts, which are useful as antithrombotic agents by inhibiting plasminogen activator inhibitor-1 (PAI-1) [wherein: R1 = (one or more) H, haloalkyl, halo, or NO2; X, Y, Z = (independently) C or N; A = bond, CH2, CO, or alkylaminocarbonyl; B = bond, alkylaminocarbonyl, CH2, or carbonylalkylester (sic); R2 = halo, NO2, CO2H or alkyl ester, haloalkyl, dialkylamide, carboxamide, alkoxyaminocarbonyl, substituted aralkylamino, aryloxy, piperazinyl, imidazolyl, or pyridinyloxy, etc.; D = N or O; R3 = (un)substituted aryl, aralkyl, carboxycyclohexyl, carboxyalkyl, piperazinyl, alkoxy, aralkoxy, carboxypyrrolidinyl, carboxypiperidinyl, carboxypyridinyloxy, carboxypyridinyl; R4 = halo, NO2, CO2H, alkyl, alkyl ester, haloalkyl, menthyloxyalkylcarbonylamino, aralkylamino, etc.; or DR3R4 = atoms to form (un)substituted piperidine or pyrrolidine ring; or R2R3 = atoms to form dioxo-substituted heterocyclic group substituted by methylphosphonic acid (when Y = Z = C); including stereoisomers and/or **pharmaceutically** acceptable salts]. In addition, the invention relates to **pharmaceutical** compns., and methods of using the compds. to treat disease-states characterized by **thrombotic** activity. Over 100 compds. are listed, all of which inhibited human PAI-1 either in vitro (recombinant PAI-1 chromogenic hydrolysis assay), ex vivo (human plasma fibrin clot lysis assay), or both, with IC50 values of less than about 15 μM. Ten formulations of invention compound II are listed. Seven synthetic prepns. are described. For instance, 2,4-dichloro-5-nitrobenzotrifluoride was doubly aminated, first with N-BOC-piperazine in the 4-position, then with Et isonipecotate in the 2-position, followed by deprotection of the BOC-protected amine, carbamoylation of the amine with 2-(trifluoromethyl)phenyl isocyanate, and saponification of the ester with LiOH in aqueous THF, to give compound II.

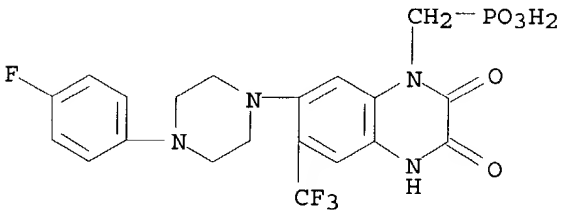
IT **608530-74-1P**, [[7-[4-(3-Chlorophenyl)piperazin-1-yl]-2,3-dioxo-6-trifluoromethyl-3,4-dihydro-2H-quinoxalin-1-yl]methyl]phosphonic acid **608530-75-2P**, [[7-[4-(4-Fluorophenyl)piperazin-1-yl]-2,3-dioxo-6-trifluoromethyl-3,4-dihydro-2H-quinoxalin-1-yl]methyl]phosphonic acid RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(drug candidate; preparation of [(triphenylmethyl)phenyl]piperazines as antithrombotic PAI-1 inhibitors)

RN 608530-74-1 CAPLUS
CN Phosphonic acid, [[7-[4-(3-chlorophenyl)-1-piperazinyl]-3,4-dihydro-2,3-dioxo-6-(trifluoromethyl)-1(2H)-quinoxalinyl]methyl]- (9CI) (CA INDEX NAME)



RN 608530-75-2 CAPLUS
CN Phosphonic acid, [[7-[4-(4-fluorophenyl)-1-piperazinyl]-3,4-dihydro-2,3-dioxo-6-(trifluoromethyl)-1(2H)-quinoxalinyl]methyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=>
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NEWS	1		Web Page URLs for STN Seminar Schedule - N. America
NEWS	2		"Ask CAS" for self-help around the clock
NEWS	3	JAN 27	Source of Registration (SR) information in REGISTRY updated and searchable
NEWS	4	JAN 27	A new search aid, the Company Name Thesaurus, available in CA/CAplus
NEWS	5	FEB 05	German (DE) application and patent publication number format changes

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 NEWS  6  MAR 03  MEDLINE and LMEDLINE reloaded
 NEWS  7  MAR 03  MEDLINE file segment of TOXCENTER reloaded
 NEWS  8  MAR 03  FRANCEPAT now available on STN
 NEWS  9  MAR 29  Pharmaceutical Substances (PS) now available on STN
 NEWS 10  MAR 29  WPIFV now available on STN
 NEWS 11  MAR 29  No connect hour charges in WPIFV until May 1, 2004
 NEWS 12  MAR 29  New monthly current-awareness alert (SDI) frequency in RAPRA
 NEWS 13  APR 26  PROMT: New display field available
 NEWS 14  APR 26  IFIPAT/IFIUDB/IFICDB: New super search and display field
                  available
 NEWS 15  APR 26  LITALERT now available on STN
 NEWS 16  APR 27  NLDB: New search and display fields available

 NEWS EXPRESS  MARCH 31 CURRENT WINDOWS VERSION IS V7.00A, CURRENT
               MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
               AND CURRENT DISCOVER FILE IS DATED 26 APRIL 2004
 NEWS HOURS    STN Operating Hours Plus Help Desk Availability
 NEWS INTER    General Internet Information
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 NEWS PHONE    Direct Dial and Telecommunication Network Access to STN
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=> file stnguide
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     2.10       2.10

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AND TECHNOLOGY CORPORATION, AND FACHINFORMATIONSZENTRUM KARLSRUHE

FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: Apr 30, 2004 (20040430/UP).

=>
Uploading
THIS COMMAND NOT AVAILABLE IN THE CURRENT FILE
Do you want to switch to the Registry File?
Choice (Y/n):
Switching to the Registry File...
Some commands only work in certain files.  For example, the EXPAND
command can only be used to look at the index in a file which has an
index.  Enter "HELP COMMANDS" at an arrow prompt (=>) for a list of
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=> FILE REGISTRY

COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     0.06       2.16
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STRUCTURE FILE UPDATES: 2 MAY 2004 HIGHEST RN 678693-82-8
DICTIONARY FILE UPDATES: 2 MAY 2004 HIGHEST RN 678693-82-8

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2004

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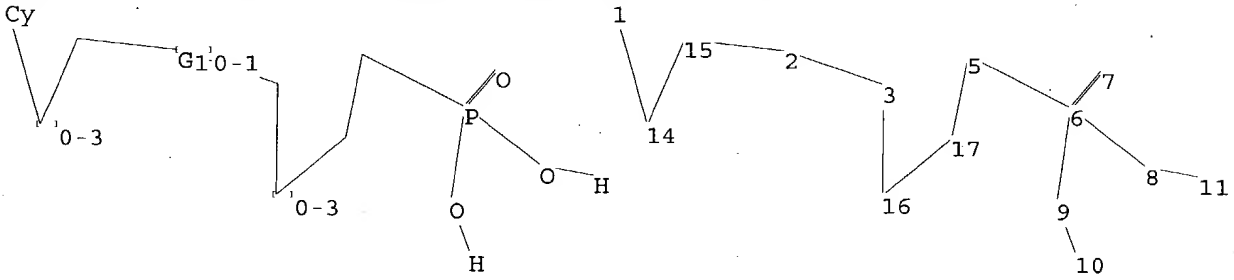

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chain bonds :
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exact/norm bonds :
1-14 2-3 2-15
exact bonds :
3-16 5-6 5-17 8-11 9-10 14-15 16-17
normalized bonds :
6-7 6-8 6-9

G1:O,S,N

Match level :
1:Atom 2:CLASS 3:CLASS 5:CLASS 6:CLASS 7:CLASS 8:CLASS 9:CLASS 10:CLASS
11:CLASS 14:CLASS 15:CLASS 16:CLASS 17:CLASS

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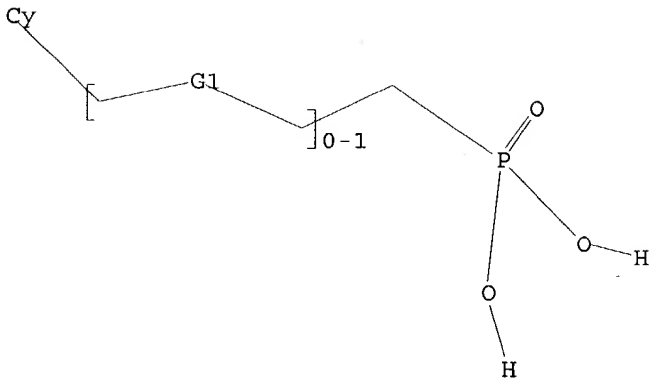
L1 STR



G1 O,S,N

Structure attributes must be viewed using STN Express query preparation.

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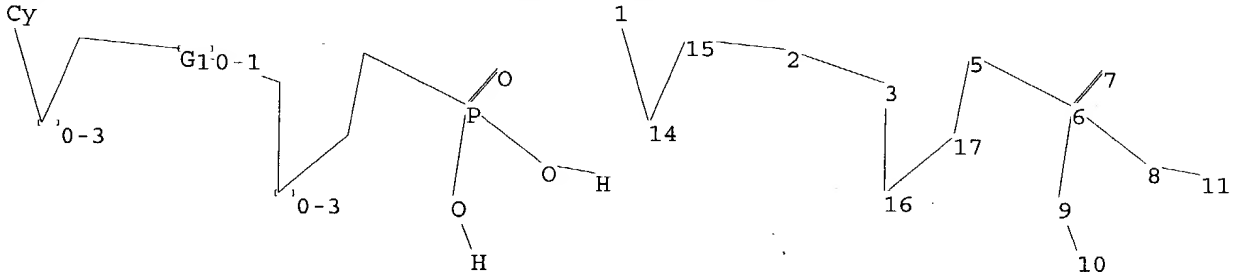

chain nodes :
1 2 3 5 6 7 8 9 10 11 14 15 16 17
chain bonds :
1-14 2-3 2-15 3-16 5-6 5-17 6-7 6-8 6-9 8-11 9-10 14-15 16-17
exact/norm bonds :
1-14 2-3 2-15
exact bonds :
3-16 5-6 5-17 8-11 9-10 14-15 16-17
normalized bonds :
6-7 6-8 6-9

G1:O,S,N

Match level :
1:Atom 2:CLASS 3:CLASS 5:CLASS 6:CLASS 7:CLASS 8:CLASS 9:CLASS 10:CLASS
11:CLASS 14:CLASS 15:CLASS 16:CLASS 17:CLASS

L2 STRUCTURE UPLOADED

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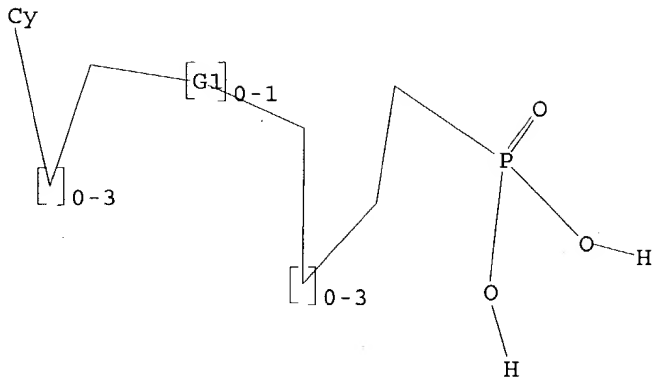
L2 HAS NO ANSWERS
L2 STR



G1 O,S,N

Structure attributes must be viewed using STN Express query preparation.

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SAMPLE SCREEN SEARCH COMPLETED -   1205 TO ITERATE

 83.0% PROCESSED    1000 ITERATIONS                                50 ANSWERS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:        22018 TO    26182
PROJECTED ANSWERS:             956 TO     1984

L3            50 SEA SSS SAM L2

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FULL SCREEN SEARCH COMPLETED -  23164 TO ITERATE

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SEARCH TIME: 00.00.01

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                                                       ENTRY    SESSION
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DICTIONARY FILE UPDATES:   2 MAY 2004  HIGHEST RN 678693-82-8

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2004
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COST IN U.S. DOLLARS

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FILE 'CAPLUS' ENTERED AT 18:10:32 ON 03 MAY 2004
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FILE COVERS 1907 - 3 May 2004 VOL 140 ISS 19
FILE LAST UPDATED: 2 May 2004 (20040502/ED)

This file contains CAS Registry Numbers for easy and accurate
substance identification.

=> s l3
L5 28 L3

=> s l5 and (blood or thromb?)
1131789 BLOOD
1163 BLOODS
1131904 BLOOD
(BLOOD OR BLOODS)
93389 THROMB?
L6 3 L5 AND (BLOOD OR THROMB?)

=> d ibib abs hitstr 1-3

L6 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:590932 CAPLUS
DOCUMENT NUMBER: 139:149413
TITLE: Selective S1P1/Edg1 receptor agonists
INVENTOR(S): Doherty, George A.; Forrest, Michael J.; Hajdu, Richard; Hale, Jeffrey J.; Li, Zhen; Mandala, Suzanne M.; Mills, Sander G.; Rosen, Hugh; Scolnick, Edward M.
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 202 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003061567	A2	20030731	WO 2003-US1120	20030114
WO 2003061567	A3	20031224		

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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2004058894	A1	20040325	US 2003-339380	20030109

PRIORITY APPLN. INFO.:

US 2002-349991P P 20020118
US 2002-362566P P 20020307
US 2002-382933P P 20020523

AB The present invention encompasses a method of treating an immunoregulatory abnormality in a mammalian patient in need of such treatment comprising administering to said patient a compound which is an agonist of the S1P1/Edg1 receptor in an amount effective for treating said immunoregulatory abnormality, wherein said compound possesses a selectivity for the S1P1/Edg1 receptor over the S1PR3/Edg3 receptor, said compound administered in an amount effective for treating said immunoregulatory abnormality. Thus, 4-HOC6H4CHO was treated with Me(CH2)7I to give 4-Me(CH2)7OC6H4CHO which was treated with H2N(CH2)3P(O)(OH)2 to give 4-Me(CH2)7OC6H4CH2NH(CH2)3P(O)(OH)2 which had an EC50 for S1P1 agonism of 1.5 nM and for S1P3 agonism of 6.0 nM.

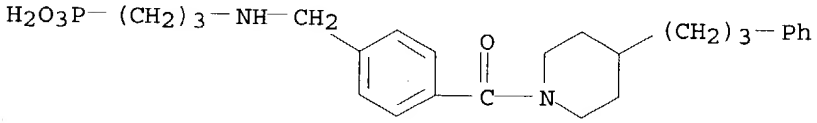
IT **569683-13-2P 569683-68-7P 569683-72-3P 569684-11-3P 569684-46-4P**

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of amino functionalized organo phosphonates or organo carboxylates as S1P1/Edg1 receptor agonists)

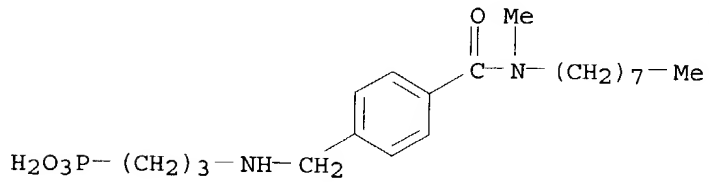
RN 569683-13-2 CAPLUS

CN Phosphonic acid, [3-[[[4-[[4-(3-phenylpropyl)-1-piperidinyl]carbonyl]phenyl]methyl]amino]propyl]- (9CI) (CA INDEX NAME)

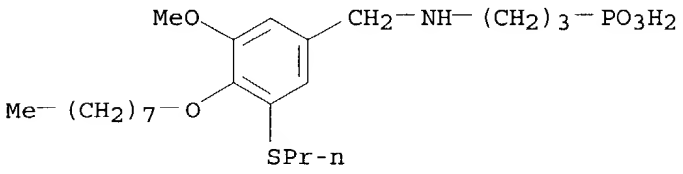


RN 569683-68-7 CAPLUS

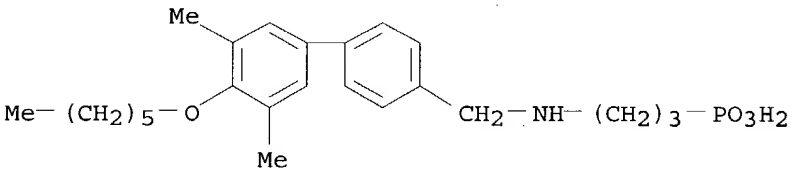
CN Phosphonic acid, [3-[[[4-[(methyloctylamino)carbonyl]phenyl]methyl]amino]propyl]- (9CI) (CA INDEX NAME)



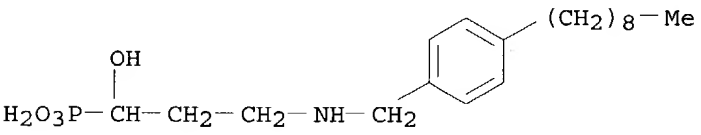
RN 569683-72-3 CAPLUS
CN Phosphonic acid, [3-[[[3-methoxy-4-(octyloxy)-5-(propylthio)phenyl]methyl]amino]propyl]- (9CI) (CA INDEX NAME)



RN 569684-11-3 CAPLUS
CN Phosphonic acid, [3-[[[4'-(hexyloxy)-3',5'-dimethyl[1,1'-biphenyl]-4-yl]methyl]amino]propyl]- (9CI) (CA INDEX NAME)



RN 569684-46-4 CAPLUS
CN Phosphonic acid, [1-hydroxy-3-[[(4-nonylphenyl)methyl]amino]propyl]- (9CI) (CA INDEX NAME)



L6 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1995:632064 CAPLUS
DOCUMENT NUMBER: 123:33653
TITLE: Preparation of (phosphonoalkyl)peptide derivatives as inhibitors of endothelin converting enzyme.
INVENTOR(S): Ishikawa, Kiyofumi; Jukami, Takehiro; Hayama, Takashi; Matsuyama, Kenji; Noguchi, Kazuhito; Yano, Mitauo
PATENT ASSIGNEE(S): Banyu Pharmaceutical Co., Ltd., Japan
SOURCE: Eur. Pat. Appl., 24 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 623625	A1	19941109	EP 1993-107203	19930504
R: CH, DE, FR, GB, IT, LI, NL				

PRIORITY APPLN. INFO.: EP 1993-107203 19930504
OTHER SOURCE(S): MARPAT 123:33653

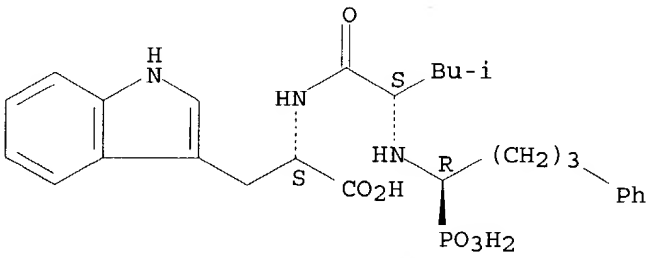
AB H2O3PCH[(CH2)nR1]NHCHR2COAOH [n = 2, 3; R1 = H, (substituted) Ph, naphthyl, indolyl, benzothienyl, benzofuryl, benzoxazolyl; R2 = alkyl, benzyl, 4-hydroxybenzyl, 3-indolylmethyl, β-phenethyl; A = Trp, Tyr, Phe, homoPhe, α-naphthylalanyl, Nω-nitroarginyl], were prepared Thus, a mixture of H-Leu-Trp-OBzl and PhCH2CH2CHO was refluxed 2 h in a Dean-Stark apparatus; dibenzyl phosphite and MeCN were added to the mixture which was stirred at 80° for 19 h to give N-[N-(1-dibenzyloxyphosphoryl-3-phenylpropyl)leucyl]tryptophan benzyl ester as a mixture of diastereomers. The diastereomers were sep. hydrogenolyzed to give, after treatment with KOH, tripotassium N-[N-(3-phenyl-1-phosphonopropyl)leucyl]tryptophan diastereomers. One of the diastereomers at 10 μM showed 88% inhibition of endothelin converting enzyme.

IT **152290-34-1P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of (phosphonolkyl)peptide derivs. as inhibitors of endothelin converting enzyme)

RN 152290-34-1 CAPLUS

CN L-Tryptophan, N-[N-(4-phenyl-1-phosphonobutyl)-L-leucyl]-, tripotassium salt, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



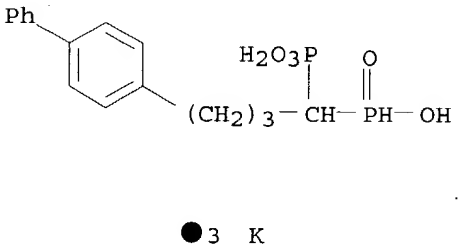
●3 K

L6 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1994:218173 CAPLUS
DOCUMENT NUMBER: 120:218173
TITLE: Preparation of hydroxyphosphinyl phosphonate squalene synthetase inhibitors
INVENTOR(S): Biller, Scott A.; Dickson, John K., Jr.
PATENT ASSIGNEE(S): E. R. Squibb and Sons, Inc., USA
SOURCE: U.S., 21 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5254544	A	19931019	US 1992-950555	19920925
CA 2104748	AA	19940326	CA 1993-2104748	19930824
JP 06199880	A2	19940719	JP 1993-236279	19930922
EP 589473	A1	19940330	EP 1993-115441	19930924
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
AU 9347561	A1	19940331	AU 1993-47561	19930924

AU 670810 B2 19960801
PRIORITY APPLN. INFO.: US 1992-950555 19920925
OTHER SOURCE(S): MARPAT 120:218173
AB HP(O)(OR2)CHR1P(O)(OR3)OR4 (R1 = lipophilic group containing >6 C atoms; R2-R4 = H, alkyl, aryl, metal ion) were prepared as squalene synthetase inhibitors (no data). Thus, bishomofarnesol (preparation given) was converted to (E,E)-14-iodo-2,6,10-trimethyl-2,6,19-tetradecatriene, which was condensed with lithiated di-Et methylphosphonate in THF at -78°-room temperature to give (E,E)-(6,10,14-trimethyl-5,9,13-pentadecatrienyl)phosphonic acid, di-Et ester. This was lithiated with BuLi in THF at -78° followed by condensation with di-Et chlorophosphate at -78°-room temperature to give, after deprotection, (E,E)-[(1-hydroxyphosphinyl)-6,10,14-trimethyl-5,9,13-pentadecatrienyl]phosphonic acid, tripotassium salt. Title compds. may also be useful in treating tumors, inhibiting formation of gallstones, lowering **blood** pressure, lowering **blood** sugar, treating diabetes, treating inflammation, and as diuretics, inotropics, and antiarthritics.
IT **153916-00-8P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as squalene synthetase inhibitor)
RN 153916-00-8 CAPLUS
CN Phosphonic acid, [4-[1,1'-biphenyl]-4-yl-1-(hydroxyphosphinyl)butyl]-, tripotassium salt (9CI) (CA INDEX NAME)



=> s l4
L7 428 L4

=> s l7 and thrombo?
66936 THROMBO?
L8 6 L7 AND THROMBO?

=> d ibib abs hitstr 1-6

L8 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:590932 CAPLUS
DOCUMENT NUMBER: 139:149413
TITLE: Selective S1P1/Edg1 receptor agonists
INVENTOR(S): Doherty, George A.; Forrest, Michael J.; Hajdu, Richard; Hale, Jeffrey J.; Li, Zhen; Mandala, Suzanne M.; Mills, Sander G.; Rosen, Hugh; Scolnick, Edward M.
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 202 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE

WO 2003061567	A2	20030731	WO 2003-US1120	20030114
WO 2003061567	A3	20031224		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2004058894	A1	20040325	US 2003-339380	20030109

PRIORITY APPLN. INFO.:

US 2002-349991P P 20020118
US 2002-362566P P 20020307
US 2002-382933P P 20020523

AB The present invention encompasses a method of treating an immunoregulatory abnormality in a mammalian patient in need of such treatment comprising administering to said patient a compound which is an agonist of the S1P1/Edg1 receptor in an amount effective for treating said immunoregulatory abnormality, wherein said compound possesses a selectivity for the S1P1/Edg1 receptor over the S1PR3/Edg3 receptor, said compound administered in an amount effective for treating said immunoregulatory abnormality. Thus, 4-HOC6H4CHO was treated with Me(CH2)7I to give 4-Me(CH2)7OC6H4CHO which was treated with H2N(CH2)3P(O)(OH)2 to give 4-Me(CH2)7OC6H4CH2NH(CH2)3P(O)(OH)2 which had an EC50 for S1P1 agonism of 1.5 nM and for S1P3 agonism of 6.0 nM.

IT **569682-66-2P 569682-67-3P 569682-68-4P 569682-69-5P 569682-70-8P 569682-71-9P 569682-72-0P 569682-73-1P 569682-74-2P 569682-75-3P 569682-77-5P 569682-78-6P 569682-87-7P 569682-89-9P 569682-91-3P 569682-93-5P 569682-95-7P 569682-97-9P 569682-99-1P 569683-01-8P 569683-03-0P 569683-05-2P 569683-07-4P 569683-09-6P 569683-11-0P 569683-13-2P 569683-15-4P 569683-30-3P 569683-32-5P 569683-34-7P 569683-39-2P 569683-49-4P 569683-51-8P 569683-55-2P 569683-57-4P 569683-59-6P 569683-61-0P 569683-63-2P 569683-67-6P 569683-68-7P 569683-70-1P 569683-72-3P 569683-74-5P 569683-76-7P 569683-78-9P 569683-81-4P 569683-82-5P 569683-87-0P 569683-89-2P 569683-90-5P 569683-92-7P 569683-94-9P 569683-96-1P 569683-99-4P 569684-01-1P 569684-03-3P 569684-05-5P 569684-07-7P 569684-09-9P 569684-11-3P 569684-13-5P 569684-15-7P 569684-17-9P 569684-19-1P 569684-21-5P 569684-23-7P 569684-25-9P 569684-26-0P 569684-27-1P 569684-28-2P 569684-30-6P 569684-32-8P 569684-34-0P 569684-39-5P 569684-41-9P 569684-46-4P 569684-47-5P 569684-48-6P 569684-49-7P 569684-50-0P 569684-78-2P 569684-80-6P 571206-09-2P 571206-10-5P 571206-11-6P 571206-12-7P 571206-13-8P 571206-14-9P 571206-15-0P 571206-16-1P 571206-17-2P**

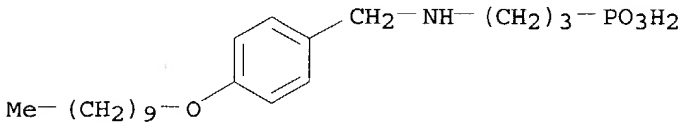
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of amino functionalized organo phosphonates or organo

carboxylates as S1P1/Edg1 receptor agonists)

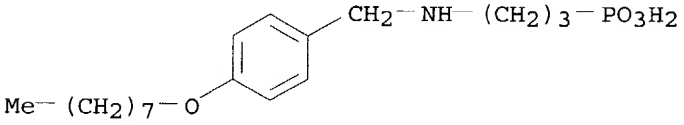
RN 569682-66-2 CAPLUS

CN Phosphonic acid, [3-[[[4-(decyloxy)phenyl]methyl]amino]propyl]- (9CI) (CA INDEX NAME)



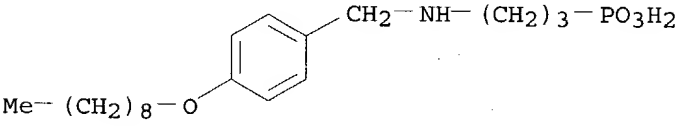
RN 569682-67-3 CAPLUS

CN Phosphonic acid, [3-[[[4-(octyloxy)phenyl]methyl]amino]propyl]- (9CI) (CA INDEX NAME)



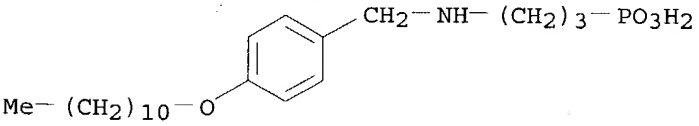
RN 569682-68-4 CAPLUS

CN Phosphonic acid, [3-[[[4-(nonyloxy)phenyl]methyl]amino]propyl]- (9CI) (CA INDEX NAME)



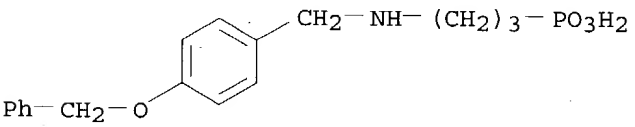
RN 569682-69-5 CAPLUS

CN Phosphonic acid, [3-[[[4-(undecyloxy)phenyl]methyl]amino]propyl]- (9CI) (CA INDEX NAME)

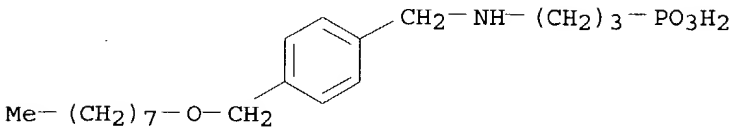


RN 569682-70-8 CAPLUS

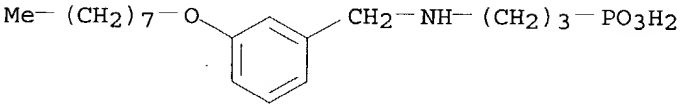
CN Phosphonic acid, [3-[[[4-(phenylmethoxy)phenyl]methyl]amino]propyl]- (9CI) (CA INDEX NAME)



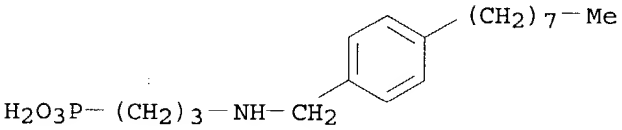
RN 569682-71-9 CAPLUS
CN Phosphonic acid, [3-[[[4-[(octyloxy)methyl]phenyl]methyl]amino]propyl]- (9CI) (CA INDEX NAME)



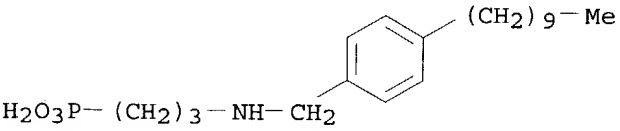
RN 569682-72-0 CAPLUS
CN Phosphonic acid, [3-[[[3-(octyloxy)phenyl]methyl]amino]propyl]- (9CI) (CA INDEX NAME)



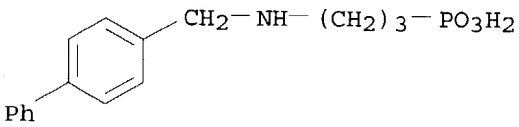
RN 569682-73-1 CAPLUS
CN Phosphonic acid, [3-[[(4-octylphenyl)methyl]amino]propyl]- (9CI) (CA INDEX NAME)



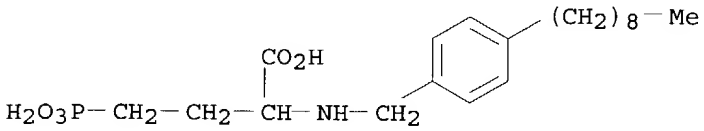
RN 569682-74-2 CAPLUS
CN Phosphonic acid, [3-[[(4-decylphenyl)methyl]amino]propyl]- (9CI) (CA INDEX NAME)



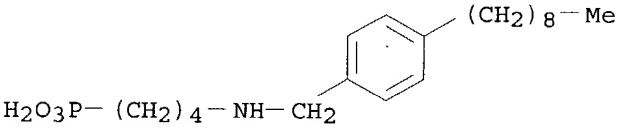
RN 569682-75-3 CAPLUS
CN Phosphonic acid, [3-[([1,1'-biphenyl]-4-ylmethyl)amino]propyl]- (9CI) (CA INDEX NAME)



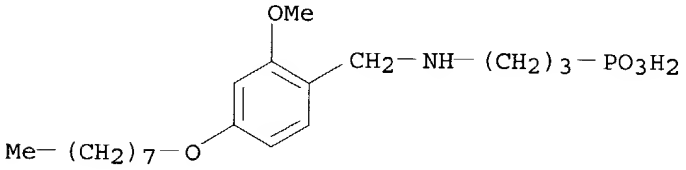
RN 569682-77-5 CAPLUS
CN Butanoic acid, 2-[[(4-nonylphenyl)methyl]amino]-4-phosphono- (9CI) (CA INDEX NAME)



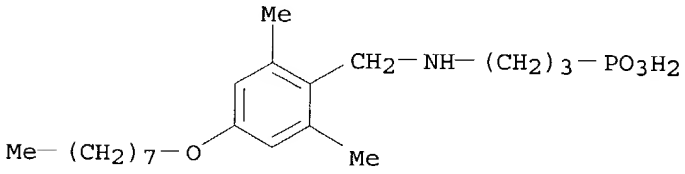
RN 569682-78-6 CAPLUS
CN Phosphonic acid, [4-[[(4-nonylphenyl)methyl]amino]butyl]- (9CI) (CA INDEX NAME)



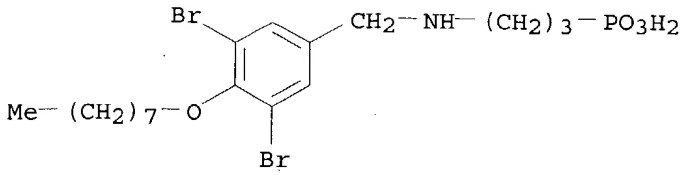
RN 569682-87-7 CAPLUS
CN Phosphonic acid, [3-[[[2-methoxy-4-(octyloxy)phenyl]methyl]amino]propyl]- (9CI) (CA INDEX NAME)



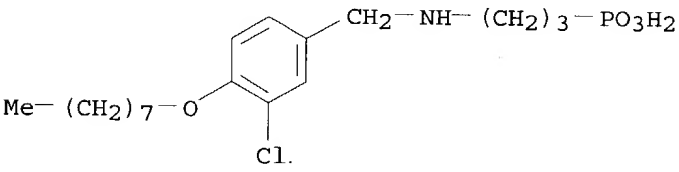
RN 569682-89-9 CAPLUS
CN Phosphonic acid, [3-[[[2,6-dimethyl-4-(octyloxy)phenyl]methyl]amino]propyl]- (9CI) (CA INDEX NAME)



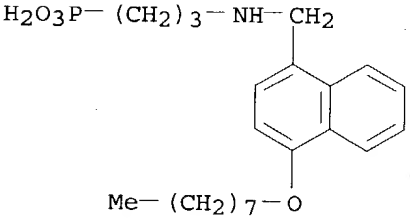
RN 569682-91-3 CAPLUS
CN Phosphonic acid, [3-[[[3,5-dibromo-4-(octyloxy)phenyl]methyl]amino]propyl]- (9CI) (CA INDEX NAME)



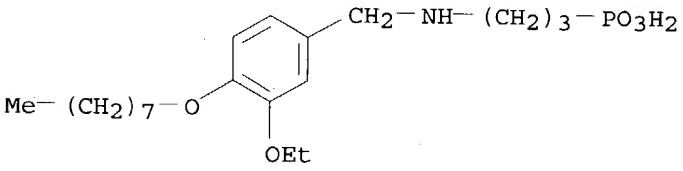
RN 569682-93-5 CAPLUS
CN Phosphonic acid, [3-[[[3-chloro-4-(octyloxy)phenyl]methyl]amino]propyl]- (9CI) (CA INDEX NAME)



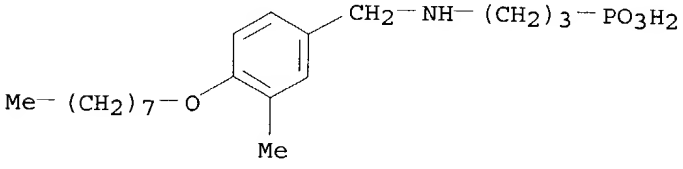
RN 569682-95-7 CAPLUS
CN Phosphonic acid, [3-[[[4-(octyloxy)-1-naphthalenyl]methyl]amino]propyl]- (9CI) (CA INDEX NAME)



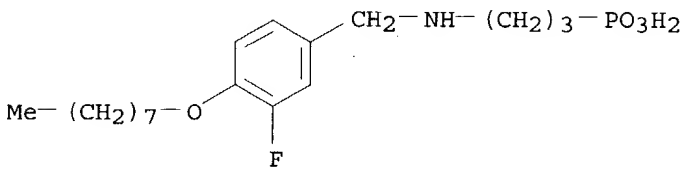
RN 569682-97-9 CAPLUS
CN Phosphonic acid, [3-[[[3-ethoxy-4-(octyloxy)phenyl]methyl]amino]propyl]- (9CI) (CA INDEX NAME)



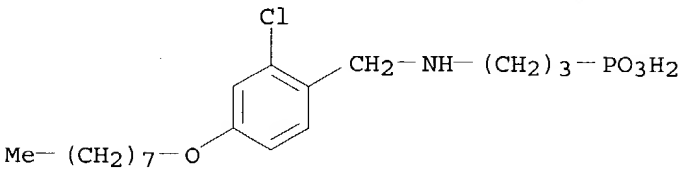
RN 569682-99-1 CAPLUS
CN Phosphonic acid, [3-[[[3-methyl-4-(octyloxy)phenyl]methyl]amino]propyl]- (9CI) (CA INDEX NAME)



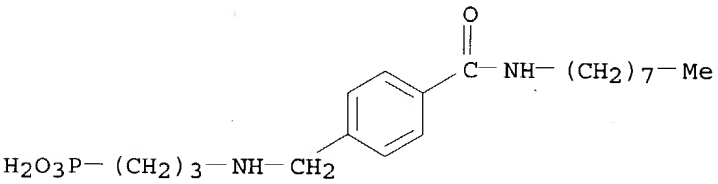
RN 569683-01-8 CAPLUS
CN Phosphonic acid, [3-[[[3-fluoro-4-(octyloxy)phenyl]methyl]amino]propyl]- (9CI) (CA INDEX NAME)



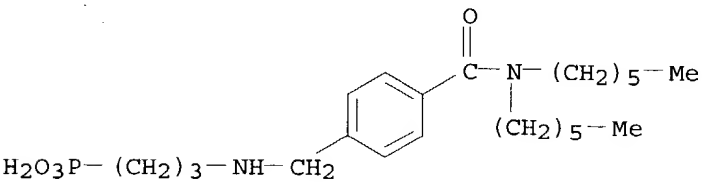
RN 569683-03-0 CAPLUS
CN Phosphonic acid, [3-[[[2-chloro-4-(octyloxy)phenyl]methyl]amino]propyl]- (9CI) (CA INDEX NAME)



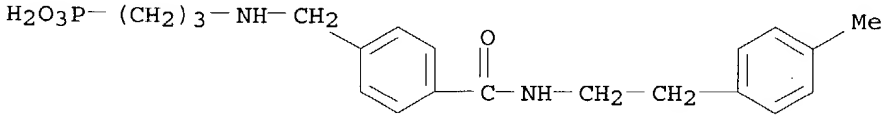
RN 569683-05-2 CAPLUS
CN Phosphonic acid, [3-[[[4-[(octylamino)carbonyl]phenyl]methyl]amino]propyl]- (9CI) (CA INDEX NAME)



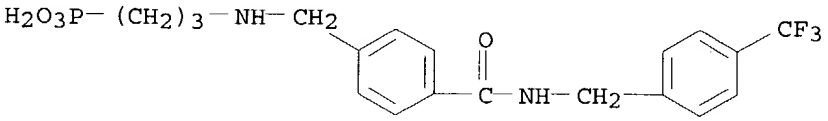
RN 569683-07-4 CAPLUS
CN Phosphonic acid, [3-[[[4-[(dihexylamino)carbonyl]phenyl]methyl]amino]propyl]- (9CI) (CA INDEX NAME)



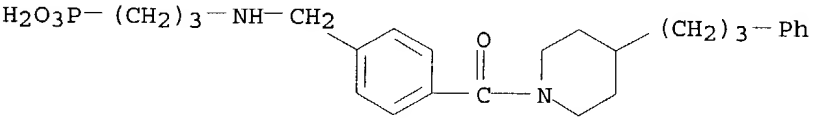
RN 569683-09-6 CAPLUS
CN Phosphonic acid, [3-[[[4-[[[2-(4-methylphenyl)ethyl]amino]carbonyl]phenyl]methyl]amino]propyl]- (9CI) (CA INDEX NAME)



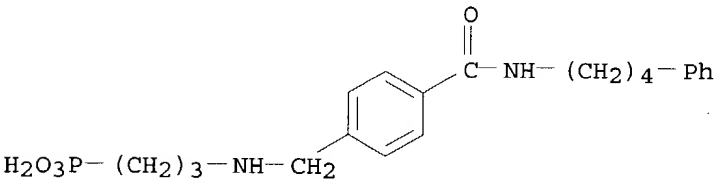
RN 569683-11-0 CAPLUS
CN Phosphonic acid, [3-[[[4-[[[[4-(trifluoromethyl)phenyl]methyl]amino]carbonyl]phenyl]methyl]amino]propyl]- (9CI) (CA INDEX NAME)



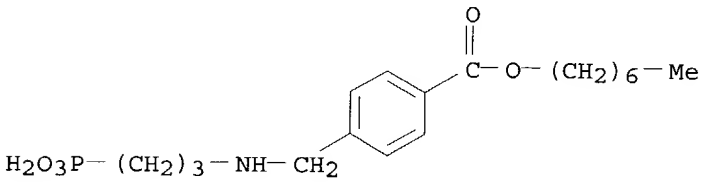
RN 569683-13-2 CAPLUS
CN Phosphonic acid, [3-[[[4-[[4-(3-phenylpropyl)-1-piperidinyl]carbonyl]phenyl]methyl]amino]propyl]- (9CI) (CA INDEX NAME)



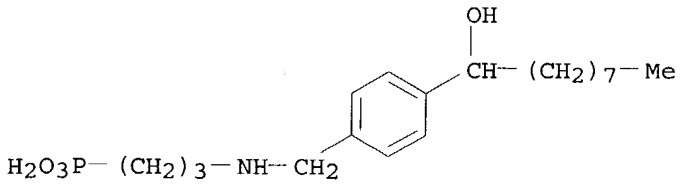
RN 569683-15-4 CAPLUS
CN Phosphonic acid, [3-[[[4-[[(4-phenylbutyl)amino]carbonyl]phenyl]methyl]amino]propyl]- (9CI) (CA INDEX NAME)



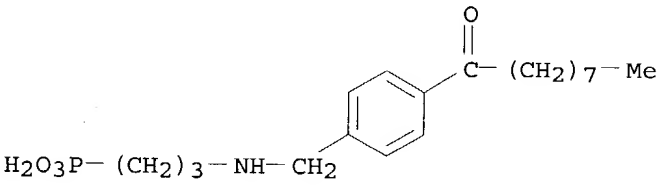
RN 569683-30-3 CAPLUS
CN Benzoic acid, 4-[[(3-phosphonopropyl)amino]methyl]-, 1-heptyl ester (9CI) (CA INDEX NAME)



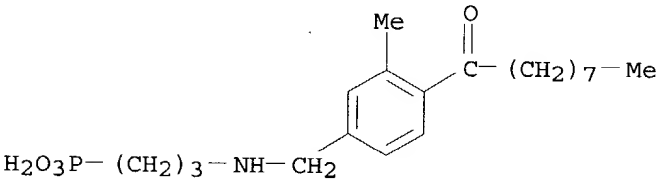
RN 569683-32-5 CAPLUS
CN Phosphonic acid, [3-[[[4-(1-hydroxynonyl)phenyl]methyl]amino]propyl]- (9CI) (CA INDEX NAME)



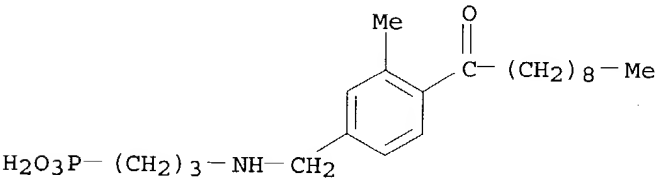
RN 569683-34-7 CAPLUS
CN Phosphonic acid, [3-[[[4-(1-oxononyl)phenyl]methyl]amino]propyl]- (9CI) (CA INDEX NAME)



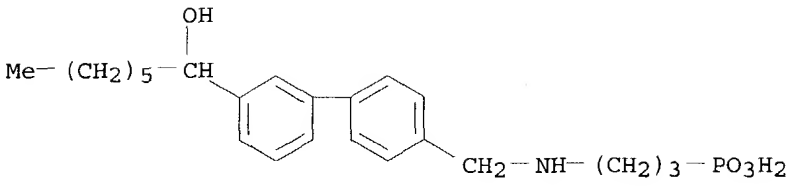
RN 569683-39-2 CAPLUS
CN Phosphonic acid, [3-[[[3-methyl-4-(1-oxononyl)phenyl]methyl]amino]propyl]- (9CI) (CA INDEX NAME)



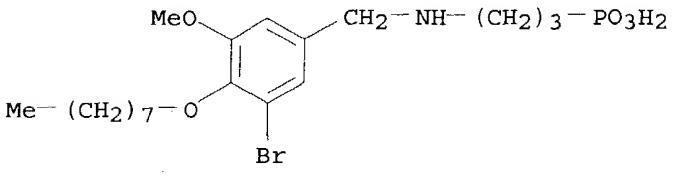
RN 569683-49-4 CAPLUS
CN Phosphonic acid, [3-[[[3-methyl-4-(1-oxodecyl)phenyl]methyl]amino]propyl]- (9CI) (CA INDEX NAME)



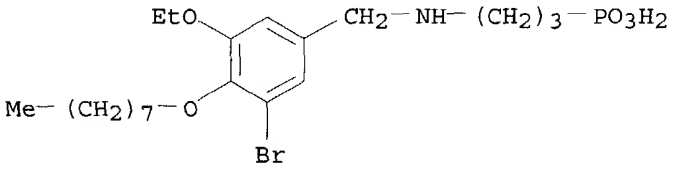
RN 569683-51-8 CAPLUS
CN Phosphonic acid, [3-[[[3'-(1-hydroxyheptyl)[1,1'-biphenyl]-4-yl]methyl]amino]propyl]- (9CI) (CA INDEX NAME)



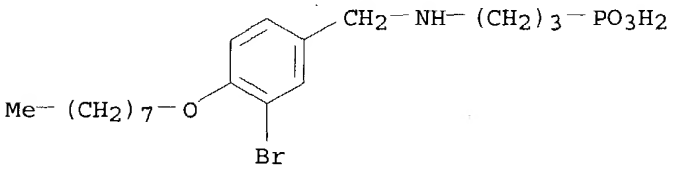
RN 569683-55-2 CAPLUS
CN Phosphonic acid, [3-[[[3-bromo-5-methoxy-4-(octyloxy)phenyl]methyl]amino]propyl]- (9CI) (CA INDEX NAME)



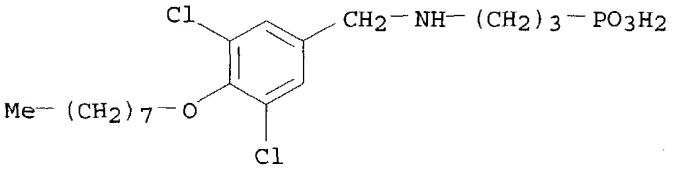
RN 569683-57-4 CAPLUS
CN Phosphonic acid, [3-[[[3-bromo-5-ethoxy-4-(octyloxy)phenyl]methyl]amino]propyl]- (9CI) (CA INDEX NAME)



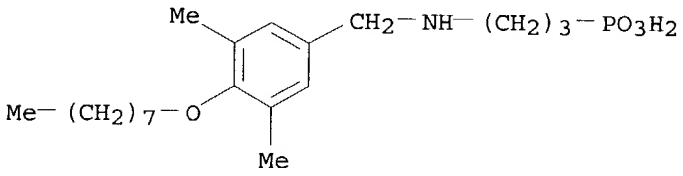
RN 569683-59-6 CAPLUS
CN Phosphonic acid, [3-[[[3-bromo-4-(octyloxy)phenyl]methyl]amino]propyl]- (9CI) (CA INDEX NAME)



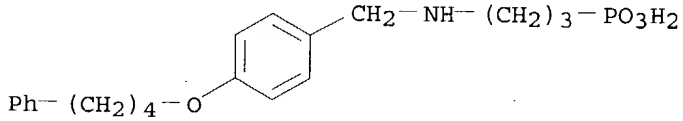
RN 569683-61-0 CAPLUS
CN Phosphonic acid, [3-[[[3,5-dichloro-4-(octyloxy)phenyl]methyl]amino]propyl]- (9CI) (CA INDEX NAME)



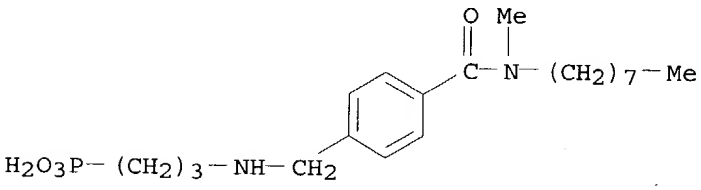
RN 569683-63-2 CAPLUS
CN Phosphonic acid, [3-[[[3,5-dimethyl-4-(octyloxy)phenyl]methyl]amino]propyl]- (9CI) (CA INDEX NAME)



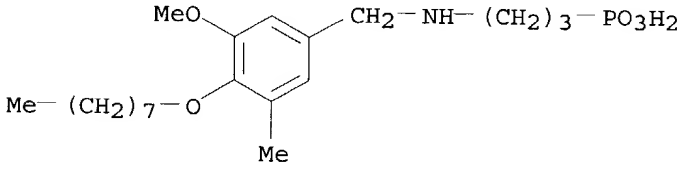
RN 569683-67-6 CAPLUS
CN Phosphonic acid, [3-[[[4-(4-phenylbutoxy)phenyl]methyl]amino]propyl]- (9CI) (CA INDEX NAME)



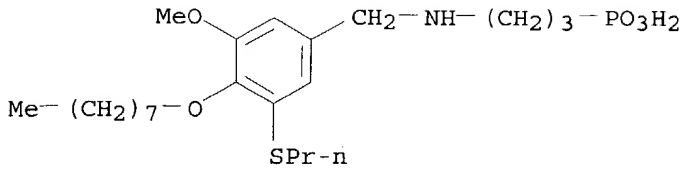
RN 569683-68-7 CAPLUS
CN Phosphonic acid, [3-[[[4-[(methyloctylamino)carbonyl]phenyl]methyl]amino]propyl]- (9CI) (CA INDEX NAME)



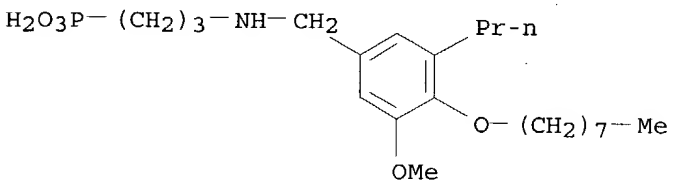
RN 569683-70-1 CAPLUS
CN Phosphonic acid, [3-[[[3-methoxy-5-methyl-4-(octyloxy)phenyl]methyl]amino]propyl]- (9CI) (CA INDEX NAME)



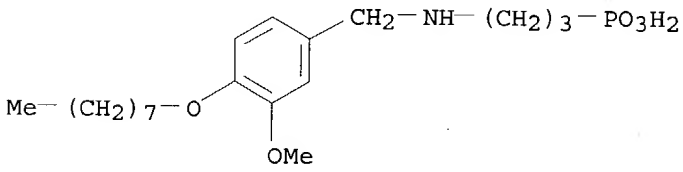
RN 569683-72-3 CAPLUS
CN Phosphonic acid, [3-[[[3-methoxy-4-(octyloxy)-5-(propylthio)phenyl]methyl]amino]propyl]- (9CI) (CA INDEX NAME)



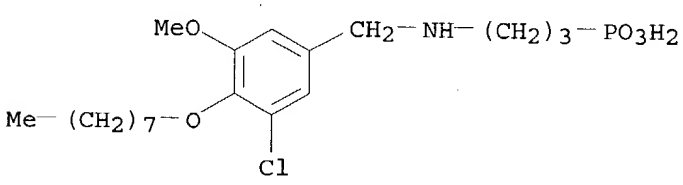
RN 569683-74-5 CAPLUS
CN Phosphonic acid, [3-[[[3-methoxy-4-(octyloxy)-5-propylphenyl]methyl]amino]propyl]- (9CI) (CA INDEX NAME)



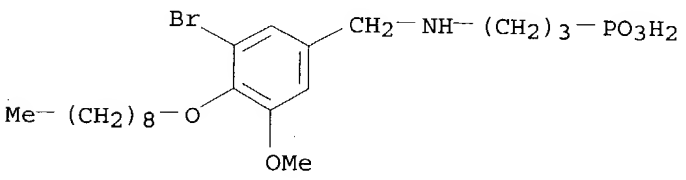
RN 569683-76-7 CAPLUS
CN Phosphonic acid, [3-[[[3-methoxy-4-(octyloxy)phenyl]methyl]amino]propyl]- (9CI) (CA INDEX NAME)



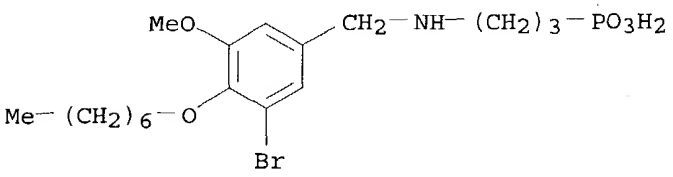
RN 569683-78-9 CAPLUS
CN Phosphonic acid, [3-[[[3-chloro-5-methoxy-4-(octyloxy)phenyl]methyl]amino]propyl]- (9CI) (CA INDEX NAME)



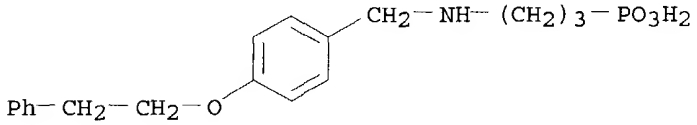
RN 569683-81-4 CAPLUS
CN Phosphonic acid, [3-[[[3-bromo-5-methoxy-4-(nonyloxy)phenyl]methyl]amino]propyl]- (9CI) (CA INDEX NAME)



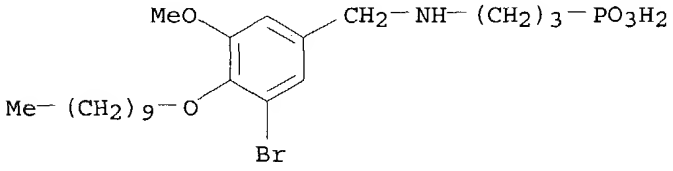
RN 569683-82-5 CAPLUS
CN Phosphonic acid, [3-[[[3-bromo-4-(heptyloxy)-5-methoxyphenyl]methyl]amino]propyl]- (9CI) (CA INDEX NAME)



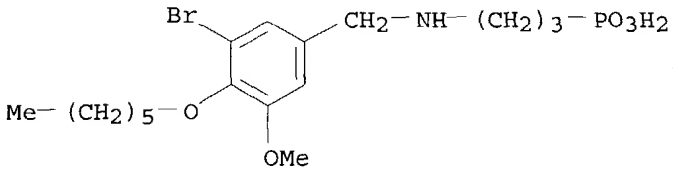
RN 569683-87-0 CAPLUS
CN Phosphonic acid, [3-[[[4-(2-phenylethoxy)phenyl]methyl]amino]propyl]- (9CI) (CA INDEX NAME)



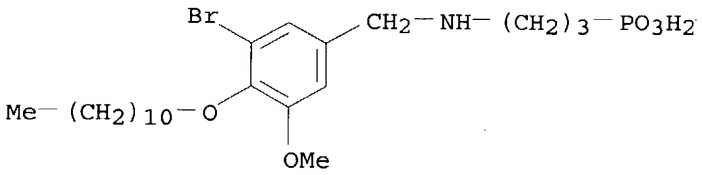
RN 569683-89-2 CAPLUS
CN Phosphonic acid, [3-[[[3-bromo-4-(decyloxy)-5-methoxyphenyl]methyl]amino]propyl]- (9CI) (CA INDEX NAME)



RN 569683-90-5 CAPLUS
CN Phosphonic acid, [3-[[[3-bromo-4-(hexyloxy)-5-methoxyphenyl]methyl]amino]propyl]- (9CI) (CA INDEX NAME)



RN 569683-92-7 CAPLUS
CN Phosphonic acid, [3-[[[3-bromo-5-methoxy-4-(undecyloxy)phenyl]methyl]amino]propyl]- (9CI) (CA INDEX NAME)

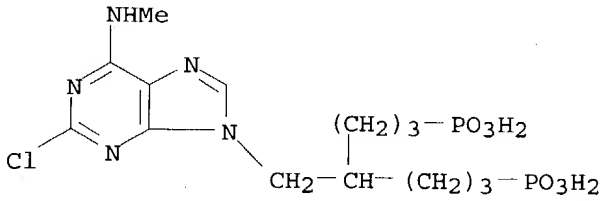

Br
CH2—NH—(CH2)3—PO3H2
Me—(CH2)10—O
OMe

ACCESSION NUMBER: 2002:884255 CAPLUS
DOCUMENT NUMBER: 138:122795
TITLE: Acyclic Analogues of Adenosine Bisphosphates as P2Y Receptor Antagonists: Phosphate Substitution Leads to Multiple Pathways of Inhibition of Platelet Aggregation
AUTHOR(S): Xu, Bin; Stephens, Andrew; Kirschenheuter, Gary; Greslin, Arthur F.; Cheng, Xiaoquin; Sennelo, Joe; Cattaneo, Marco; Zighetti, Maddalena L.; Chen, Aishe; Kim, Soon-Ai; Kim, Hak Sung; Bischofberger, Norbert; Cook, Gary; Jacobson, Kenneth A.
CORPORATE SOURCE: Molecular Recognition Section, Laboratory of Bioorganic Chemistry, National Institute of Diabetes Digestive and Kidney Diseases, National Institutes of Health, Bethesda, MD, 20892-0810, USA
SOURCE: Journal of Medicinal Chemistry (2002), 45(26), 5694-5709
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 138:122795

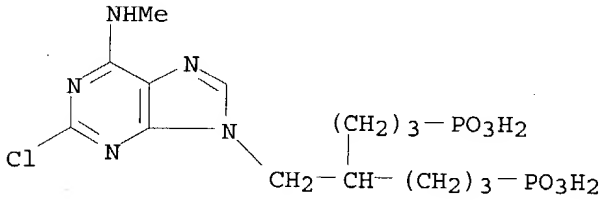
AB Activation by ADP of both P2Y1 and P2Y12 receptors in platelets contributes to platelet aggregation, and antagonists at these receptor subtypes have antithrombotic properties. In an earlier publication, the authors have characterized the SAR as P2Y1 receptor antagonists of acyclic analogs of adenine nucleotides, containing two phosphate groups on a sym. branched aliphatic chain, attached at the 9-position of adenine. In this study, the authors have focused on anti-aggregatory effects of P2Y antagonists related to a 2-chloro-N6-methyladenine-9-(2-methylpropyl) scaffold, containing uncharged substitutions of the phosphate groups. For the known nucleotide (cyclic and acyclic) bisphosphate antagonists of P2Y1 receptors, there was a significant correlation between inhibition of aggregation induced by 3.3 μM ADP in rat platelets and inhibition of P2Y1 receptor-induced phospholipase C (PLC) activity previously determined in turkey erythrocytes. Substitution of the phosphate groups with non-hydrolyzable phosphonate groups preserved platelet anti-aggregatory activity. Substitution of one of the phosphate groups with O-acyl greatly reduced the inhibitory potency, which tended to increase upon replacement of both phosphate moieties of the acyclic derivs. with uncharged (e.g., ester) groups. In the series of nonsym. substituted monophosphates, the optimal antagonist potency occurred with the phenylcarbamate group. Among sym. diester derivs., the optimal antagonist potency occurred with the di(phenylacetyl) group. A dipivaloyl derivative, a representative uncharged diester, inhibited ADP-induced aggregation in both rat (KI 3.6 μM) and human platelets. It antagonized the ADP-induced inhibition of the cAMP pathway in rat platelets (IC50 7 μM) but did not affect hP2Y1 receptor-induced PLC activity measured in transfected astrocytoma cells. The authors propose that the uncharged derivs. are acting as antagonists of a parallel pro-aggregatory receptor present on platelets, i.e., the P2Y12 receptor. Thus, different substitution of the same nucleoside scaffold can target either of two P2Y receptors in platelets.

IT **491611-68-8P**
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(preparation and SAR of acyclic analogs of adenine nucleotides as platelet aggregation inhibitors and P2Y receptor targeting)

RN 491611-68-8 CAPLUS
CN Phosphonic acid, [4-[[2-chloro-6-(methylamino)-9H-purin-9-yl]methyl]-1,7-heptanediyl]bis- (9CI) (CA INDEX NAME)



IT **491611-99-5P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and SAR of acyclic analogs of adenine nucleotides as platelet aggregation inhibitors and P2Y receptor targeting)
RN 491611-99-5 CAPLUS
CN Phosphonic acid, [4-[[2-chloro-6-(methylamino)-9H-purin-9-yl]methyl]-1,7-heptanediyl]bis-, tetrasodium salt (9CI) (CA INDEX NAME)



●4 Na

REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:900841 CAPLUS
DOCUMENT NUMBER: 134:37031
TITLE: FVIIA/TF activity inhibiting compounds
INVENTOR(S): Jakobsen, Palle; Persson, Egon
PATENT ASSIGNEE(S): Novo Nordisk A/S, Den.
SOURCE: PCT Int. Appl., 25 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000077246	A2	20001221	WO 2000-DK316	20000613
WO 2000077246	A3	20010222		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1192270	A2	20020403	EP 2000-934951	20000613

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO

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US 6238878	B1	20010529	US 2000-616010	20000713
US 6444434	B1	20020903	US 2001-844828	20010427
US 2003073695	A1	20030417	US 2002-262826	20021002

PRIORITY APPLN. INFO.:

DK 1999-840	A	19990614
US 1999-139714P	P	19990617
DK 1999-910	A	19990625
US 1999-141416P	P	19990629
DK 1999-1241	A	19990903
US 1999-152863P	P	19990908
US 2000-577731	B1	20000523
WO 2000-DK316	W	20000613
US 2000-616010	A1	20000713

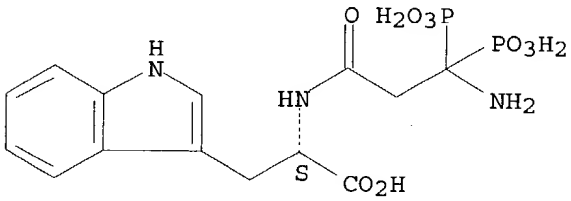
AB The invention relates to compds. inhibiting the activation of FX to FXa by TF/FVIIa. The compds. are anticoagulants. The invention also relates to a method of identifying a drug candidate.

IT **313236-58-7**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(FVIIA/TF activity inhibiting compds.)

RN 313236-58-7 CAPLUS

CN L-Tryptophan, 3,3-diphosphono-β-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L8 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1999:643377 CAPLUS

DOCUMENT NUMBER: 132:50221

TITLE: Design and synthesis of thrombin inhibitors: Analogues of MD-805 with reduced stereogenicity and improved potency

AUTHOR(S): Brundish, Derek; Bull, Alice; Donovan, Vera; Fullerton, Joseph D.; Garman, Sheila M.; Hayler, Judy F.; Janus, Diana; Kane, Peter D.; McDonnell, Mark; Smith, Garrick P.; Wakeford, Robert; Walker, Clive V.; Howarth, Graham; Hoyle, William; Allen, Mark C.; Ambler, John; Butler, Keith; Talbot, Mark D.

CORPORATE SOURCE: Department of Chemistry Department of Biology and Drug Discovery Support, Novartis Horsham Research Centre, Horsham West Sussex, RH12 5AB, UK

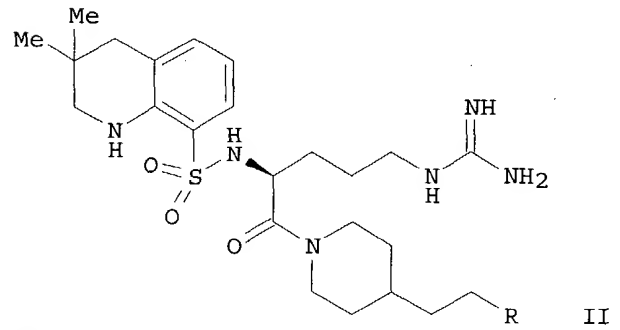
SOURCE: Journal of Medicinal Chemistry (1999), 42(22), 4584-4603
CODEN: JMCMAR; ISSN: 0022-2623

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

GI



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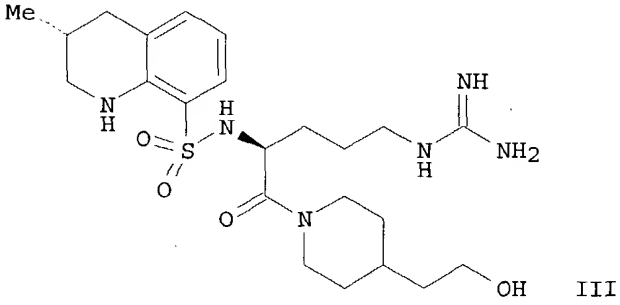


III

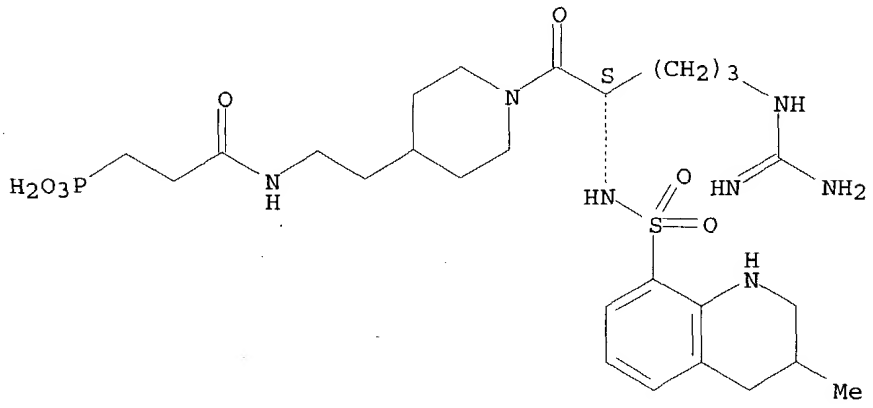
AB Mitsubishi's MD-805 (I), a potent and selective inhibitor of thrombin which contains four stereogenic centers, has been the starting point for an optimization program. A systematic synthetic study resulted in thrombin inhibitors with achiral centers but with a 10-fold increase in potency. A number of C-4 substituted piperidines were prepared and examined as replacements for the 2-carboxy-4-methylpiperidine moiety in I; replacement by 4-(fluoroethyl)piperidine, among others, provided inhibitors, e.g. (guanidinopentanoyl)piperidine II (R = F), of increased potency. An enantioselective route was developed to (R)-3-methyl-1,2,3,4-tetrahydroquinolinesulfonyl chloride. Inhibitors containing this enantiomerically pure fragment, e.g. III, had similar potency to the racemic material and provided support, with modeling studies, for the preparation of gem 3,3-disubstituted compds. A series of inhibitors containing the 3,3-dimethyl-1,2,3,4-tetrahydroquinolinesulfonyl moiety were prepared and showed a similar activity profile as the monomethyl series. The combination of 3,3-dimethyl-1,2,3,4-tetrahydroquinolinesulfonyl, 4-(2-fluoroethyl)piperidine, and arginine in II (R = F) had a Ki of 6 nM compared to I with Ki = 85 nM. In animal models of both venous and arterial **thrombosis**, one inhibitor II (R = OH) produced a dose-dependent inhibition of thrombus formation that was superior to that of I.

IT **252986-16-6P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and thrombin inhibiting activity of piperidine (tetrahydroquinolinylsulfonyl)argininamide MD-805 analogs)

RN 252986-16-6 CAPLUS

CN Phosphonic acid, [3-[[2-[1-[(2S)-5-[(aminoiminomethyl)amino]-1-oxo-2-[[(1,2,3,4-tetrahydro-3-methyl-8-quinolinyl)sulfonyl]amino]pentyl]-4-piperidinyl]ethyl]amino]-3-oxopropyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 71 THERE ARE 71 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1995:632064 CAPLUS
DOCUMENT NUMBER: 123:33653
TITLE: Preparation of (phosphonoalkyl)peptide derivatives as inhibitors of endothelin converting enzyme.
INVENTOR(S): Ishikawa, Kiyofumi; Jukami, Takehiro; Hayama, Takashi; Matsuyama, Kenji; Noguchi, Kazuhito; Yano, Mitauo
PATENT ASSIGNEE(S): Banyu Pharmaceutical Co., Ltd., Japan
SOURCE: Eur. Pat. Appl., 24 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

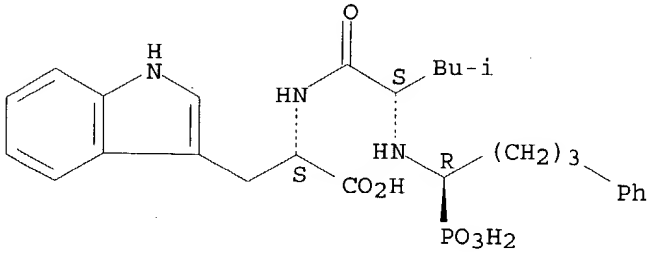
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 623625	A1	19941109	EP 1993-107203	19930504
R: CH, DE, FR, GB, IT, LI, NL				

PRIORITY APPLN. INFO.: EP 1993-107203 19930504
OTHER SOURCE(S): MARPAT 123:33653

AB H2O3PCH[(CH2)nR1]NHCHR2COAOH [n = 2, 3; R1 = H, (substituted) Ph, naphthyl, indolyl, benzothienyl, benzofuryl, benzoxazolyl; R2 = alkyl, benzyl, 4-hydroxybenzyl, 3-indolylmethyl, β-phenethyl; A = Trp, Tyr, Phe, homoPhe, α-naphthylalanyl, Nω-nitroarginyl], were prepared Thus, a mixture of H-Leu-Trp-OBzl and PhCH2CH2CHO was refluxed 2 h in a Dean-Stark apparatus; dibenzyl phosphite and MeCN were added to the mixture which was stirred at 80° for 19 h to give N-[N-(1-dibenzyloxyphosphoryl-3-phenylpropyl)leucyl]tryptophan benzyl ester as a mixture of diastereomers. The diastereomers were sep. hydrogenolyzed to give, after treatment with KOH, tripotassium N-[N-(3-phenyl-1-phosphonopropyl)leucyl]tryptophan diastereomers. One of the diastereomers at 10 μM showed 88% inhibition of endothelin converting enzyme.

IT **152290-34-1P 152376-10-8P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of (phosphonolkyl)peptide derivs. as inhibitors of endothelin converting enzyme)
RN 152290-34-1 CAPLUS
CN L-Tryptophan, N-[N-(4-phenyl-1-phosphonobutyl)-L-leucyl]-, tripotassium salt, (R)- (9CI) (CA INDEX NAME)

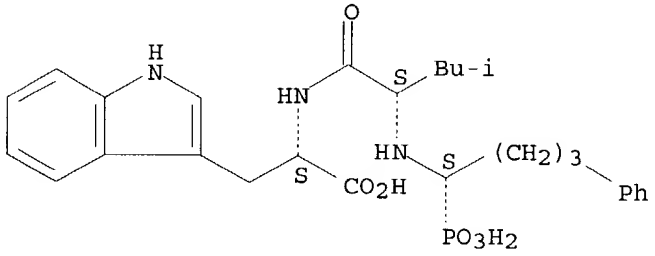
Absolute stereochemistry.



●3 K

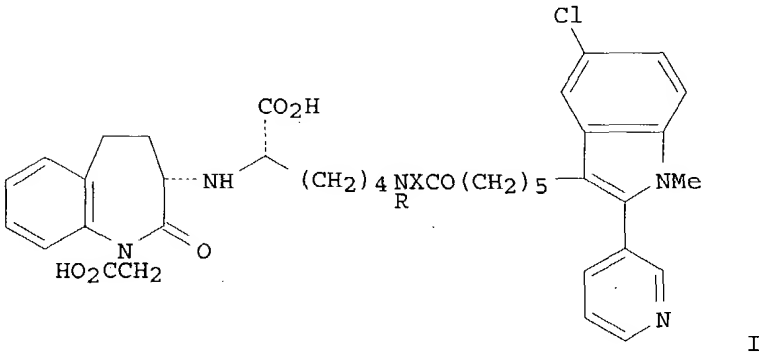
RN 152376-10-8 CAPLUS
CN L-Tryptophan, N-[N-(4-phenyl-1-phosphonobutyl)-L-leucyl]-, tripotassium salt, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



●3 K

L8 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1994:655622 CAPLUS
DOCUMENT NUMBER: 121:255622
TITLE: Dual Angiotensin Converting Enzyme/**Thromboxane** Synthase Inhibitors
AUTHOR(S): Ksander, Gary M.; Erion, Mark; Yuan, Andrew M.; Diefenbacher, Clive G.; El-Chehabi, Lena; Cote, Don; Levens, Nigel
CORPORATE SOURCE: Pharmaceuticals Division, CIBA-GEIGY Corporation, Summit, NJ, 07901, USA
SOURCE: Journal of Medicinal Chemistry (1994), 37(12), 1823-32
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



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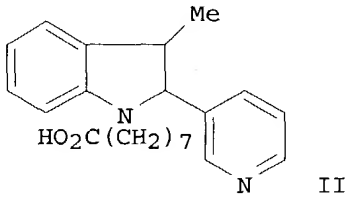


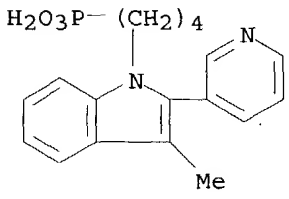
II

AB A variety of compds. were prepared to determine whether dual angiotensin converting enzyme (ACE)/**thromboxane** synthase (TxS) inhibition could be obtained in the same mol. These compds. would be used to explore the concept that a dual inhibitor would have superior antihypertensive activity in the spontaneous hypertensive rat (SHR) compared to an ACE inhibitor. Potent in vitro dual ACE and TxS inhibition was obtained in the same mol. with five series of compds. Potent blood pressure lowering in the SHR was observed after oral administration of benzazepines I [R = CH2CH2OH, X = bond; R = H, X = 1,4-piperidinediyl]. However, a correlation between blood pressure lowering and the A1 pressor response inhibition was not observed The blood pressure-lowering actions of enalapril were significantly potentiated by concurrent administration of the indole II, a **thromboxane** synthase inhibitor. Anal. of the area under the curve for 24 h showed nearly a doubling of the blood pressure-lowering effect.

IT **158387-45-2P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and angiotensin converting enzyme and **thromboxane** synthase inhibition by)

RN 158387-45-2 CAPLUS

CN Phosphonic acid, [4-[3-methyl-2-(3-pyridinyl)-1H-indol-1-yl]butyl]- (9CI) (CA INDEX NAME)



L12 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1995:632064 CAPLUS
DOCUMENT NUMBER: 123:33653
TITLE: Preparation of (phosphonoalkyl)peptide derivatives as inhibitors of endothelin converting enzyme.
INVENTOR(S): Ishikawa, Kiyofumi; Jukami, Takehiro; Hayama, Takashi; Matsuyama, Kenji; Noguchi, Kazuhito; Yano, Mitauo
PATENT ASSIGNEE(S): Banyu Pharmaceutical Co., Ltd., Japan
SOURCE: Eur. Pat. Appl., 24 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 623625	A1	19941109	EP 1993-107203	19930504
R: CH, DE, FR, GB, IT, LI, NL				

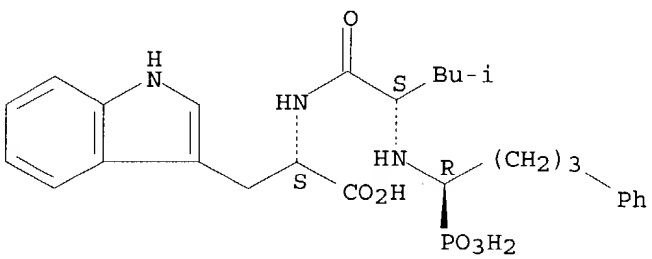
PRIORITY APPLN. INFO.: EP 1993-107203 19930504
OTHER SOURCE(S): MARPAT 123:33653

AB H2O3PCH[(CH2)nR1]NHCHR2COAOH [n = 2, 3; R1 = H, (substituted) Ph, naphthyl, indolyl, benzothienyl, benzofuryl, benzoxazolyl; R2 = alkyl, benzyl, 4-hydroxybenzyl, 3-indolylmethyl, β-phenethyl; A = Trp, Tyr, Phe, homoPhe, α-naphthylalanyl, Nω-nitroarginyl], were prepared Thus, a mixture of H-Leu-Trp-OBzl and PhCH2CH2CHO was refluxed 2 h in a Dean-Stark apparatus; dibenzyl phosphite and MeCN were added to the mixture which was stirred at 80° for 19 h to give N-[N-(1-dibenzyloxyphosphoryl-3-phenylpropyl)leucyl]tryptophan benzyl ester as a mixture of diastereomers. The diastereomers were sep. hydrogenolyzed to give, after treatment with KOH, tripotassium N-[N-(3-phenyl-1-phosphonopropyl)leucyl]tryptophan diastereomers. One of the diastereomers at 10 μM showed 88% inhibition of endothelin converting enzyme.

IT **152290-34-1P 152376-10-8P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of (phosphonolkyl)peptide derivs. as inhibitors of endothelin converting enzyme)

RN 152290-34-1 CAPLUS
CN L-Tryptophan, N-[N-(4-phenyl-1-phosphonobutyl)-L-leucyl]-, tripotassium salt, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

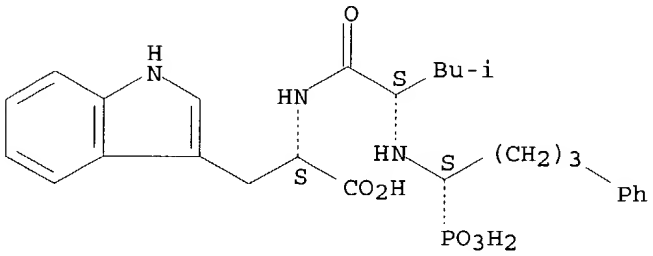


●3 K

RN 152376-10-8 CAPLUS

CN L-Tryptophan, N-[N-(4-phenyl-1-phosphonobutyl)-L-leucyl]-, tripotassium salt, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



●3 K

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L12 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1999:643377 CAPLUS
DOCUMENT NUMBER: 132:50221
TITLE: Design and synthesis of thrombin inhibitors: Analogues of MD-805 with reduced stereogenicity and improved potency
AUTHOR(S): Brundish, Derek; Bull, Alice; Donovan, Vera; Fullerton, Joseph D.; Garman, Sheila M.; Hayler, Judy F.; Janus, Diana; Kane, Peter D.; McDonnell, Mark; Smith, Garrick P.; Wakeford, Robert; Walker, Clive V.; Howarth, Graham; Hoyle, William; Allen, Mark C.; Ambler, John; Butler, Keith; Talbot, Mark D.
CORPORATE SOURCE: Department of Chemistry Department of Biology and Drug Discovery Support, Novartis Horsham Research Centre, Horsham West Sussex, RH12 5AB, UK
SOURCE: Journal of Medicinal Chemistry (1999), 42(22), 4584-4603
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
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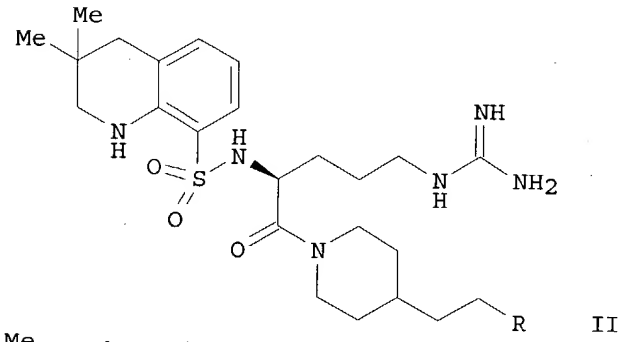

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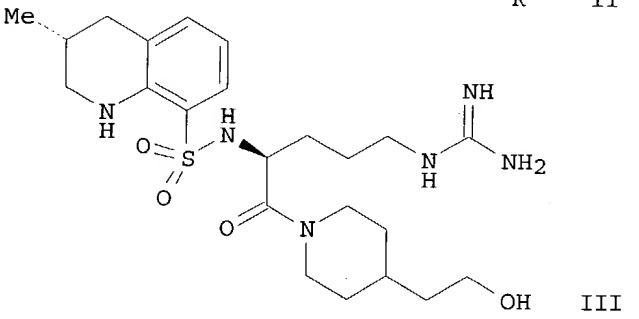


III

AB Mitsubishi's MD-805 (I), a potent and selective inhibitor of thrombin which contains four stereogenic centers, has been the starting point for an optimization program. A systematic synthetic study resulted in thrombin inhibitors with achiral centers but with a 10-fold increase in potency. A number of C-4 substituted piperidines were prepared and examined as replacements for the 2-carboxy-4-methylpiperidine moiety in I; replacement by 4-(fluoroethyl)piperidine, among others, provided inhibitors, e.g. (guanidinopentanoyl)piperidine II (R = F), of increased potency. An enantioselective route was developed to (R)-3-methyl-1,2,3,4-tetrahydroquinolinesulfonyl chloride. Inhibitors containing this enantiomerically pure fragment, e.g. III, had similar potency to the racemic material and provided support, with modeling studies, for the preparation of gem 3,3-disubstituted compds. A series of inhibitors containing the

3,3-dimethyl-1,2,3,4-tetrahydroquinolinesulfonyl moiety were prepared and showed a similar activity profile as the monomethyl series. The combination of 3,3-dimethyl-1,2,3,4-tetrahydroquinolinesulfonyl, 4-(2-fluoroethyl)piperidine, and arginine in II (R = F) had a Ki of 6 nM compared to I with Ki = 85 nM. In animal models of both venous and arterial **thrombosis**, one inhibitor II (R = OH) produced a dose-dependent inhibition of thrombus formation that was superior to that of I.

IT **252986-16-6P**

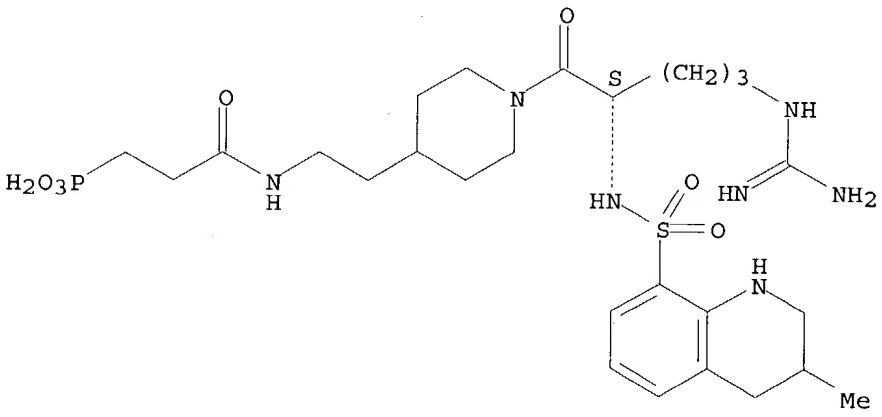
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(preparation and thrombin inhibiting activity of piperidine (tetrahydroquinolinylsulfonyl)argininamide MD-805 analogs)

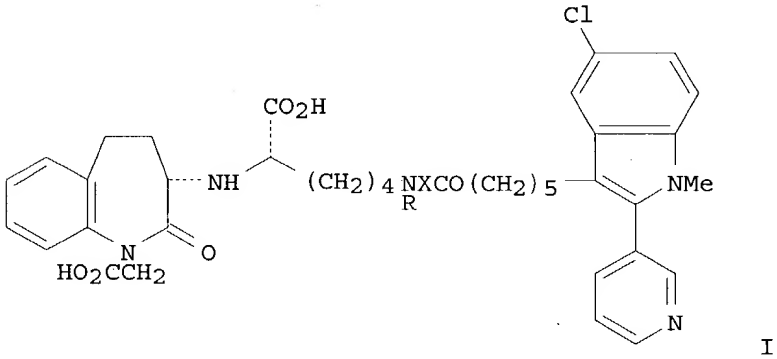
RN 252986-16-6 CAPLUS

CN Phosphonic acid, [3-[[2-[1-[(2S)-5-[(aminoiminomethyl)amino]-1-oxo-2-[[(1,2,3,4-tetrahydro-3-methyl-8-quinolinyl)sulfonyl]amino]pentyl]-4-piperidinyl]ethyl]amino]-3-oxopropyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L8 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1994:655622 CAPLUS
DOCUMENT NUMBER: 121:255622
TITLE: Dual Angiotensin Converting Enzyme/**Thromboxane** Synthase Inhibitors
AUTHOR(S): Ksander, Gary M.; Erion, Mark; Yuan, Andrew M.; Diefenbacher, Clive G.; El-Chehabi, Lena; Cote, Don; Levens, Nigel
CORPORATE SOURCE: Pharmaceuticals Division, CIBA-GEIGY Corporation, Summit, NJ, 07901, USA
SOURCE: Journal of Medicinal Chemistry (1994), 37(12), 1823-32
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



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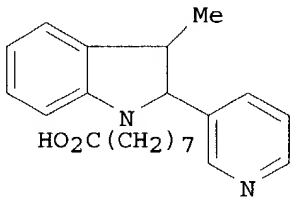
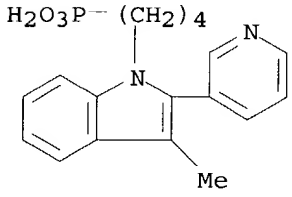


II

AB A variety of compds. were prepared to determine whether dual angiotensin converting enzyme (ACE)/**thromboxane** synthase (TxS) inhibition could be obtained in the same mol. These compds. would be used to explore the concept that a dual inhibitor would have superior antihypertensive activity in the spontaneous hypertensive rat (SHR) compared to an ACE inhibitor. Potent in vitro dual ACE and TxS inhibition was obtained in the same mol. with five series of compds. Potent blood pressure lowering in the SHR was observed after oral administration of benzazepines I [R = CH2CH2OH, X = bond; R = H, X = 1,4-piperidinediyl]. However, a correlation between blood pressure lowering and the A1 pressor response inhibition was not observed The blood pressure-lowering actions of enalapril were significantly potentiated by concurrent administration of the indole II, a **thromboxane** synthase inhibitor. Anal. of the area under the curve for 24 h showed nearly a doubling of the blood pressure-lowering effect.

IT **158387-45-2P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and angiotensin converting enzyme and **thromboxane** synthase inhibition by)
RN 158387-45-2 CAPLUS
CN Phosphonic acid, [4-[3-methyl-2-(3-pyridinyl)-1H-indol-1-yl]butyl]- (9CI)

(CA INDEX NAME)

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=> s thromboxane and thrombosis
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           2534 THROMBOXANES
          14724 THROMBOXANE
                  (THROMBOXANE OR THROMBOXANES)
          18016 THROMBOSIS
L9          623 THROMBOXANE AND THROMBOSIS

=> s thromboxane (s) thrombosis
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           2534 THROMBOXANES
          14724 THROMBOXANE
                  (THROMBOXANE OR THROMBOXANES)
          18016 THROMBOSIS
L10         239 THROMBOXANE (S) THROMBOSIS

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